Review

Journal of
Biomedical Nanotechnology
Vol. 10, 2778–2805, 2014
www.aspbs.com/jbn

Magnetic Resonance Imaging Findings for Dyslexia: A Review

Ahmed Elnakib[1], Ahmed Soliman[1], Matthew Nitzken[1], Manuel F. Casanova[2],
Georgy Gimel'farb[3], and Ayman El-Baz[1,*]

[1] *Bioimaging Laboratory, Department of Bioengineering, University of Louisville, Louisville, KY 40292, USA*
[2] *Department of Psychiatry and Behavioral Sciences, University of Louisville, Louisville, KY 40202, USA*
[3] *Department of Computer Science, University of Auckland, Auckland 1142, New Zealand*

Developmental dyslexia is a brain disorder that is associated with a disability to read, which affects both the behavior and the learning abilities of children. Recent advances in MRI techniques have enabled imaging of different brain structures and correlating the results to clinical findings. The goal of this paper is to cover these imaging studies in order to provide a better understanding of dyslexia and its associated brain abnormalities. In addition, this survey covers the noninvasive MRI-based diagnostics methods that can offer early detection of dyslexia. We focus on three MRI techniques: structural MRI, functional MRI, and diffusion tensor imaging. Structural MRI reveals dyslexia-associated volumetric and shape-based abnormalities in different brain structures (e.g., reduced grey matter volumes, decreased cerebral white matter gyrifications, increased corpus callosum size, and abnormal asymmetry of the cerebellum and planum temporale structures). Functional MRI reports abnormal activation patterns in dyslexia during reading operations (e.g., aggregated studies observed under-activations in the left hemisphere fusiform and supramarginal gyri and over-activation in the left cerebellum in dyslexic subjects compared with controls). Finally, diffusion tensor imaging reveals abnormal orientations in areas within the white matter micro-structures of dyslexic brains (e.g., aggregated studies reported a reduction of the fraction anisotropy values in bilateral areas within the white matter). Herein, we will discuss all of these MRI findings focusing on various aspects of implemented methodologies, testing databases, as well as the reported findings. Finally, the paper addresses the correlation between the MRI findings in the literature, various aspects of research challenges, and future trends in this active research field.

KEYWORDS: *Dyslexia, Survey, Brain, Findings, MRI, Functional MRI, Diffusion Tensor MRI.*

CONTENTS

Introduction 2778
Structural MRI 2781
  Grey Matter 2781
  White Matter 2783
  Planum Temporale and Cerebellum 2785
  Corpus Callosum (CC) 2786
Diffusion Tensor Imaging (DTI) 2788
Functional MRI 2789
Discussion and Conclusion 2797
  Research Challenges 2798
  Trends 2799
  References 2799

INTRODUCTION

Developmental brain disorders are among the most interesting and challenging research areas in mod-ern neuroscience. Dyslexia is an extremely complicated example of such a disorder that affects anywhere between 4% to 10% of the general population.[1] Dyslexia is characterized by the failure to develop age-appropriate reading skills in spite of a normal intelligence level and adequate reading instructions.[2–5] Perceptual problems in dyslexia seemingly result from an inability to retrieve correct verbal labels for phonemes,[6,7] which makes it difficult to deconstruct words into constituent sounds and match written words to spoken language.[8] Educational interventions that teach phoneme awareness have shown better results in dealing with reading disorders than other programs.[9–11] Although considerable progress has been made towards the identification of

---

*Author to whom correspondence should be addressed.
Email: aselba01@louisville.edu
Received: 14 January 2014
Accepted: 28 January 2014

1550-7033/2014/10/2778/028 doi:10.1166/jbn.2014.1895

effective instructional practices, our knowledge regarding the underlying pathology and pathophysiological mechanisms remains fragmentary.[12, 13]

Case studies in dyslexia have suggested various flaws in the circuitry of the visual cortex and connectivity/synchronicity between different brain regions.[14, 15] Research studies suggest that the alteration in connectivity between brain regions is basically derived from microscopic abnormalities in the minicolumn's basic ontogenetic pattern.[16] Minicolumns are the basic functional unit of the cerebral cortex, and each brain has hundreds of millions of them.[17] The areal expansion of the cerebral cortex across species (encephalization) presumably occurs through an increased number of minicolumns. Therefore, it is not surprising that some of the gross changes observed in putative minicolumnopathies include variations in brain volume, gyrification, and size of the corpus callosum (CC). Recent neuropathological case reports suggest the presence of a minicolumnopathy in dyslexia.[18, 19] Consistent with this observation, some structural magnetic

Ahmed Elnakib PhD, received his B.Sc. and M.S. degrees from Mansoura University, Egypt, in 2003 and 2007, respectively. He received his Ph.D. degree from university of Louisville, USA, in 2013. His current research includes developing new computer aided diagnostic systems, image modeling, image segmentation and registration, and shape analysis of medical structures. He has authored or coauthored more than 50 technical articles, appeared in world-renown journals including Medical Physics and IEEE TITB. Mr. Elnakib is a regular reviewer for a number of technical journals including Medical Image Analysis, IEEE TMI and IEEE TIP. He was the recipient of the John Houchens Prize for the Outstanding Dissertation, 2013.

Ahmed Soliman has received his B.Sc. and M.S. degrees in Computer Engineering from Mansoura University, Mansoura, Egypt. In December 2011 he joined the BioImaging Laboratory at University of Louisville as a research assistant. He has actively been working on design of computer aided-diagnostic systems for segmentation and parallel algorithms development for N-dimensional images in the field of medical image analysis. He has received the U.S. National Science Foundation travel grant to attend the International Symposium on Biomedical Imaging in 2013.

Matthew Nitzken has received his B.S. and M.Eng. degrees from the University of Louisville, Louisville, KY. He is currently a Doctoral Candidate in the Electrical and Computer Engineering program at the University of Louisville. He has a strong focus in the fields of Shape Analysis, computer-aided detection and diagnosis, complex brain disorders, and he has worked extensively in the brain, lung, heart and prostate. He has more than 20 publications and book chapters, 6 patents, and has had the opportunity to present in countries around the world, including the USA, Germany, Spain, and Japan.

Manuel F. Casanova MD, is the Gottfried and Gisela Kolbe Endowed Chair in Psychiatry for the University of Louisville. He was a Magisterial Speaker at the World Autism Congress in 2010 and the recipient of an EUREKA award from the NIMH. Dr. Casanova has received the titles of Stanley Scholar from the United States and an Honorary Professor degree from the University of Krasnoyarsk, Russia. He is one of the founding members for the International Autism Institute. He serves on the Editorial Board of 20 journals and has published over 200 peer reviewed articles and 70 book chapters.

Georgy Gimel'farb PhD, Professor of Computer Science and a co-Director of the Intelligent Vision Systems Laboratory, University of Auckland, New Zealand. His research interests include probabilistic image modelling, statistical pattern recognition, texture analysis in medical and remotely sensed images, and computer stereo vision. In 1997 he received a prestigious State Premium of Ukraine in Science and Technology for fundamental and applied results in image and signal recognition. He authored or co-authored more than 45 journal articles, 260 papers in peer-reviewed conference proceedings, 65 book chapters, two textbooks and four books, including the monograph "Image Textures and Gibbs Random Fields" (Kluwer Academic, 1999).

Ayman El-Baz PhD, Associate Professor and University Scholar in the Department of Bioengineering at the University of Louisville, K. Y. Dr. El-Baz has twelve years of hands-on experience in the fields of bioimaging modeling and computer-assisted diagnostic systems. His work has been reported at several prestigious international conferences (e.g., CVPR, MICCAI, etc.) and in journals (e.g., IEEE TMI, IEEE TIP, IEEE TBME, IEEE TITB, Brain, etc.). His work related to novel image analysis techniques for lung cancer and autism diagnosis have earned him multiple awards, including: first place at the annual Research Louisville 2002 to 2012 meetings. Dr. El-Baz has authored or coauthored more than 300 technical articles.

resonance imaging (MRI)-based studies have shown that dyslexic patients have a reduced brain volume, decreased gyrification, and increased CC volume relative to the total brain size.[20] In this survey, we expand on these microscopic findings by describing reported MRI findings for dyslexia. The review aims to improve the understanding of possible causal abnormalities, their topography, and proposed MRI-based diagnostics methods for dyslexia.

Multiple studies have identified different brain structures (e.g., grey matter, white matter, cerebellum, planum temporale, and CC structures) involved in abnormal neural development associated with dyslexia[21–23] (see Fig. 1). A general MRI-based dyslexia framework to detect such abnormalities is illustrated in Figure 2. The input of the framework is the MRI data (e.g., structural MRI, functional MRI (fMRI), or diffusion tensor imaging (DTI)). The first step of the framework is to remove the noise and enhance the images using image filtering and noise removal techniques. Second, the target brain structure is selected either manually or using a specified segmentation technique. Finally, different metrics can be derived from the selected brain structure to indicate an abnormality associated with dyslexia. An abnormality is identified if a candidate metric showed a significant difference between its reported values tested on two sample groups of normal and dyslexic subjects. This survey addresses the different types of brain abnormalities and presents the different metrics used to describe them using MRI techniques.

Examples of these metrics include the different volumetric and shape metrics that are extracted using structural MRI. For example, structural MRI studies reported altered brain volumes in the brains of dyslexic individuals found on specific regions of the brain (e.g., in the grey matter, white matter, cerebellum, and CC structures). In addition, shape metrics have been derived from structural MRI, such as the reported abnormality in CC thickness and asymmetry of the cerebellum in dyslexic subjects with respect to controls. fMRI can provide measures for the under- or over-activations in dyslexic subjects compared with controls, when stimulated with different reading operations. Using DTI, the diffusion parameters, such as the fraction anisotropy (FA), are candidate metrics to describe the abnormalities associated with dyslexia.

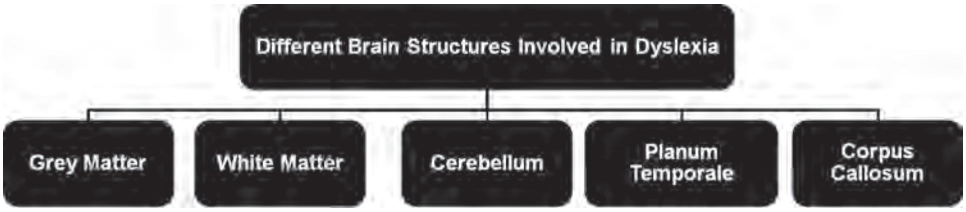


Figure 1. **Different brain structures that are involved in dyslexia.**

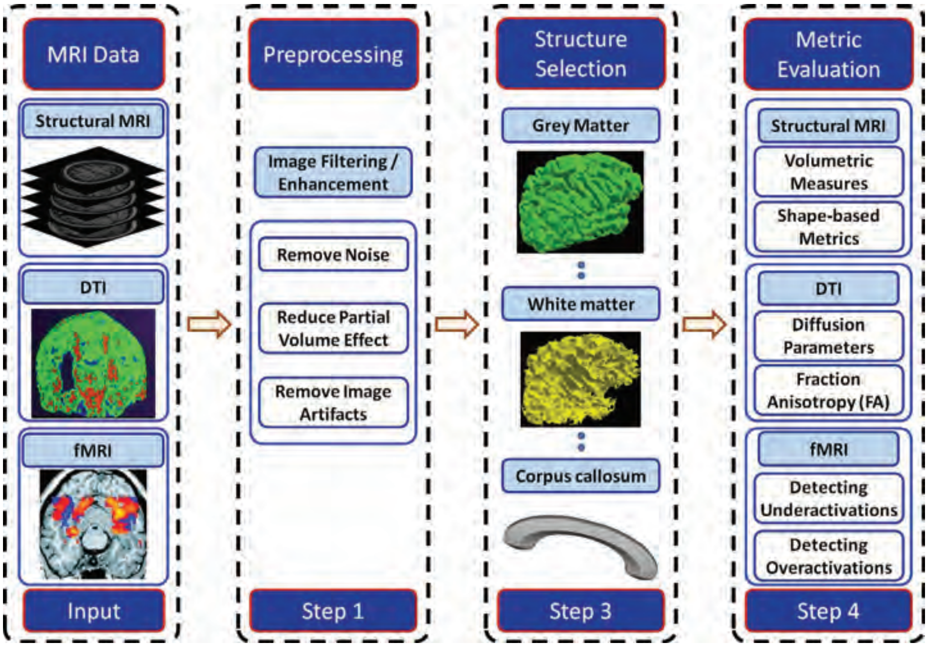


Figure 2. A general framework for analyzing MRI images in order to detect brain abnormalities associated with dyslexia.

Figure 3 summarizes the different reported findings that can be observed using different MRI techniques.

The rest of this paper is organized as follows. Sections 1–3 overview the different findings of structural MRI, DTI, and fMRI studies on dyslexia, respectively. This will include the various aspects of implemented methodologies, testing databases, as well as the reported findings for each study. Section 4 addresses the correlation between the reported MRI findings in the literature and outlines the research challenges that face the current MRI-based diagnostic methods as well as the suggested trends to solve these challenges.

STRUCTURAL MRI

MRI is a medical imaging modality that is based on the principles of nuclear magnetic resonance (NMR) spectroscopy.[24] The main strength of MRI is that it offers the best soft tissue contrast among all image modalities. This makes MRI the most powerful noninvasive tool for clinical diagnosis and a very useful modality in imaging the brain anatomy.[25] Due to the structural MRI ability to image brain soft tissues with high contrast, it has been used extensively to reveal dyslexia-associated abnormalities in different brain structures as well as to derive volumetric and shape metrics to describe these abnormalities.[26, 27] Below, the structural MRI findings for dyslexia are described for each brain structure that has been investigated, i.e., the grey matter, white matter, cerebellum, planum temporale, and CC (see Fig. 4).

Grey Matter

The cerebral cortex or grey matter contains the nerve cells responsible for routing sensory and/or motor stimuli

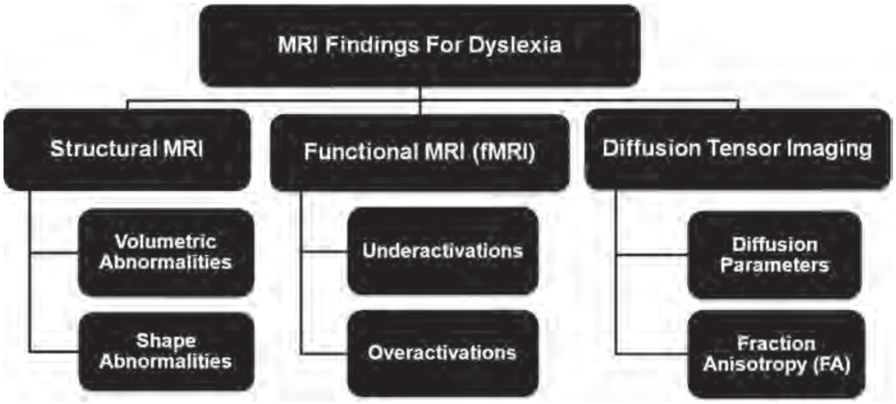
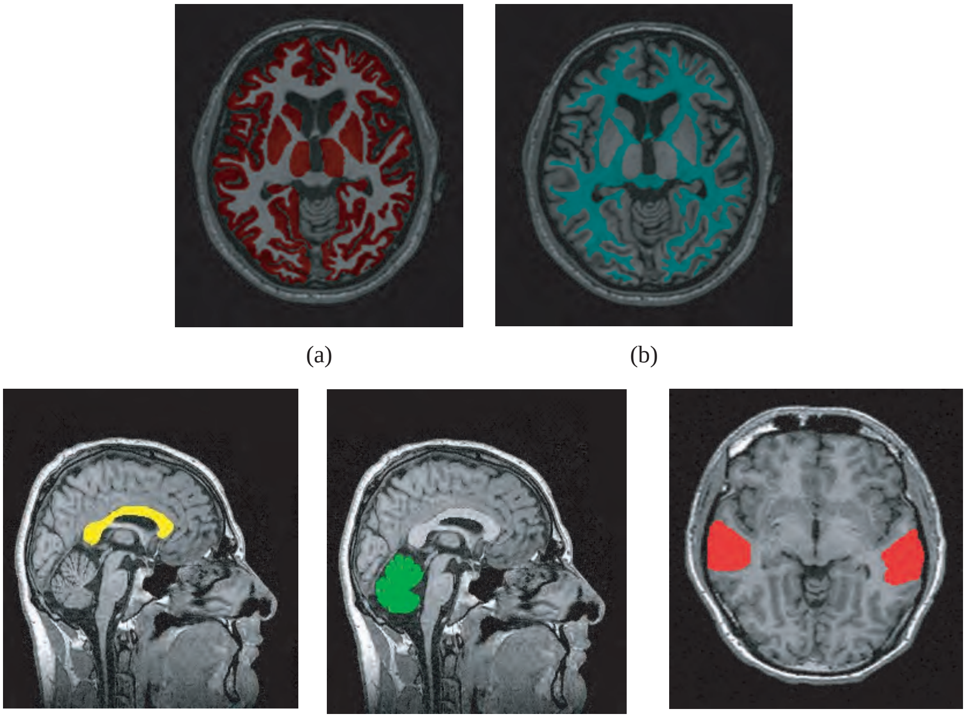


Figure 3. A taxonomy of the different findings that can be obtained using the different MRI techniques such as structural MRI, fMRI, and DTI.



(a) (b)

(c) (d) (e)

Figure 4. Different brain structures that are involved in dyslexia as appears in structural MRI: (a) grey matter (delineated in dark-red), (b) white matter (delineated in dark-cyan), (c) corpus callosum (delineated in yellow), (d) cerebellum (delineated in green), and (e) planum temporale (delineated in red).

through the central nervous system (see Fig. 5). One hypothesis suggests that the grey matter density in specific regions (e.g., reading areas) of the brains of dyslexic individuals is altered. Following this hypothesis, altered brain regions were identified with a voxel-based morphometry (VBM)[28–37] using software packages, such as BrainImage software[28] and statistical parametric mapping (SPM) software.[29, 30, 32–37] The idea behind the VBM approach is to normalize the brain stereotactically to a common space (e.g., an atlas with predefined anatomic subregions) and use voxel statistics to identify anatomical brain regions of altered grey matter density. Using the VBM analysis, altered grey matter density was identified in the left temporal lobes,[28] left and right fusiform gyrus, bilateral anterior cerebellum, and right supramarginal gyrus.[29] Brown et al.[30] reported decreased volumes of the gray matter in the left temporal lobe, bilaterally in the temporoparietooccipital juncture, frontal lobe, caudate, thalamus, and cerebellum of dyslexic brains. Brambati et al.[31] reported focal abnormalities in gray matter volume bilaterally in the planum temporale, inferior temporal cortex, and cerebellar nuclei. Silani et al.[32] identified altered grey and white matter density in the left middle and inferior temporal gyri and the left arcuate fasciculus. Eckert et al.[33] identified gray matter volume differences in the left and right lingual gyrus, left inferior parietal lobule, and cerebellum. Vinckenbosch et al.[34] reported reduced gray matter volumes in both temporal lobes of dyslexic brains, particularly in the middle and inferior temporal gyri of the left temporal lobe. In addition, the study reported increased gray matter density bilaterally in the precentral gyri. Hoeft et al.[35] reported reduced gray matter volume in the left parietal region in dyslexic brains. Steinbrink et al.[37] reported reduced gray matter volumes in the superior temporal gyrus of both hemispheres of dyslexic brains. Pernet et al.[38] reported alterations of the grey matter in the left superior temporal gyrus, occipital-temporal cortices, and lateral/medial cerebellum.

Schultz et al.[39] emphasized the role of sex and age when analyzing the brain abnormalities associated with dyslexia. Following this way of thinking, Evans et al.[40] investigated grey matter abnormalities associated with sex and age in dyslexia. They used a VBM approach to study the grey matter differences between four groups: 28 men (mean age 43 years), 26 women (mean age 34 years), 30 boys (mean age 10 years), and 34 girls (mean age 10 years). For the first group (men), reduced grey matter volumes were reported in both the left middle/inferior temporal gyri and right postcentral/supramarginal gyri of the brains. In the second group (women), reduced grey matter volumes were reported in the right precuneus and paracentral lobule/medial frontal gyrus. In boys, a reduced grey matter volume was reported in the left inferior parietal cortex (supramarginal/angular gyri). Finally, differences in girls

Figure 5. **A visualization figure for the brain showing the grey matter, white matter, and corpus callosum structures.**

were seen within the right central sulcus and adjacent gyri, and the left primary visual cortex. The study suggested the importance of considering sex and age when analyzing grey matter abnormalities.

In addition, VBM analysis has been used to investigate other findings associated with dyslexia. For example, Jednoróg et al.[41] used a VBM approach to investigate the existence of anatomical markers associated with distinct cognitive impairments of dyslexia. VBM analysis has been applied to four groups: a group of 35 controls and three groups of dyslexic subtypes (total of 46 dyslexic children).

These groups were classified based on the cognitive deficits: phonological, rapid naming, magnocellular/dorsal, and auditory attention shifting. VBM analysis revealed grey matter volume clusters specific to each studied group including areas of left inferior frontal gyrus, cerebellum, right putamen, and bilateral parietal cortex. Krafnick et al.[42] used VBM analysis to investigate possible volumetric changes in the grey matter following intensive reading intervention in dyslexic children, which resulted in significant gains in reading skills. The study on 11 dyslexic children showed that the intervention was accompanied by an increase in grey matter volume, reported in the left anterior fusiform gyrus/hippocampus, left precuneus, right hippocampus and right anterior cerebellum. Raschle et al.[43] used VBM analysis to investigate if the structural alterations in the brain are present before reading is taught. This study, performed on 20 children, reported a reduction in gray matter volumes in the left occipitotemporal, bilateral parietotemporal regions, left fusiform gyrus, and right lingual gyrus for pre-reading children with a family history of dyslexia compared to children without a family history of dyslexia. The study suggested that the reported brain alteration in dyslexia may be present at birth or develop in early childhood prior to reading onset.

Instead of examining the volumetric changes in the grey matter densities in the brain, several studies have investigated the shape abnormalities in the brain cortex associated with dyslexia.[44–46] For example, Nitzken et al.[44] used spherical harmonic (SH) analysis to detect the brain cortex variability between dyslexic and normal brains. The SHs (a linear combination of special basis functions) were used to represent the shape complexity of the 3D surface of the brain in controls and dyslexic individuals. The shape complexity of the brain was described using the estimated number of the SHs to delineate the brain cortex[44, 47–49] (see Fig. 6). This number was used to classify the brains as normal or dyslexic. Their experiments suggest that the estimated number of the SHs is a promising supplement to the current screening methods for dyslexia. A study by Williams et al.[45] using the SH analysis in Ref. [44], observed that dyslexic brains exhibit less surface complexity than controls (see Fig. 6). Altarelli et al.[46] analyzed the cortical thickness on the ventral occipitotemporal regions, due to their defined functional response to visual categories. The cortical thickness was estimated for each participant using Freesurfer software.[50, 51] The study reported a reduction in the cortical thickness in the left hemisphere regions of dyslexic brain, which are responsive to words. Table I summarizes the current MRI-based systems for the detection of dyslexia-associated grey matter abnormalities.

White Matter

The white matter of the brain connects different areas of the gray matter within the nervous system[52] (see Fig. 5). Several studies[32, 53, 56] have attempted to identify how the

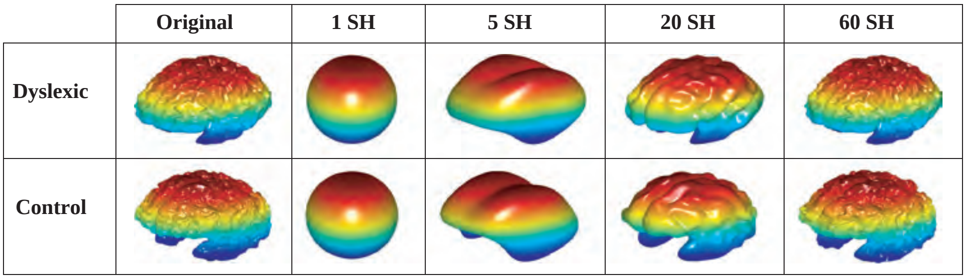


Figure 6. **Method proposed by Nitzken et al.[44] for the approximation of the 3D brain cortex shape for dyslexic and normal subjects.**

Table I. Image-based systems for the detection of dyslexia-associated grey matter abnormalities using structural MRI. For each study, the number of subjects, the method, and the study findings are reported.

Study/ref.	Data	Method	Findings
Eliez et al.[28]	30 subjects: 16 dyslexic and 14 control	Voxel-based morphometry (VBM)	• Altered grey matter density was reported in the left temporal lobes
Brown et al.[30]	30 subjects: 16 dyslexic and 14 control	Voxel-based morphometry (VBM)	• Reduced gray matter volumes were reported in dyslexic brains in the left temporal lobe, bilaterally in the temporoparietooccipital juncture, in the frontal lobe, caudate, thalamus, and cerebellum
Silani et al.[32]	64 subjects: 32 dyslexic and 32 control	Voxel-based morphometry (VBM)	• Altered grey matter density was reported in the left middle and inferior temporal gyri and the left arcuate fasciculus
Eckert et al.[33]	26 subjects: 13 dyslexic and 13 control	Voxel-based morphometry (VBM)	• Altered grey matter density was reported in the left and right lingual gyrus, left inferior parietal lobule, and cerebellum
Vinckenbosch et al.[34]	24 subjects: 10 dyslexic and 14 control	Voxel-based morphometry (VBM)	• Reduced gray matter volumes were reported in both temporal lobes of dyslexic brains, particularly in the middle and inferior temporal gyri of the left temporal lobe. Increased gray matter density was reported in the precentral gyri bilaterally
Kronbichler et al.[29]	28 subjects: 13 dyslexic and 15 control	Voxel-based morphometry (VBM)	• Altered grey matter density was reported in the left and right fusiform gyrus, bilateral anterior cerebellum, and right supramarginal gyrus
Steinbrink et al.[37]	16 subjects: 8 dyslexic and 8 control	Voxel-based morphometry (VBM)	• Reduced gray matter volumes were reported in the superior temporal gyrus of both hemispheres of dyslexic brains
Pernet et al.[38]	77 subjects: 38 dyslexic and 39 control	Voxel-based morphometry (VBM)	• Altered grey matter volumes were reported in the left superior temporal gyrus, occipital-temporal cortices, and lateral/medial cerebellum
Krafnick et al.[42]	11 dyslexic children	Voxel-based morphometry (VBM)	• Reading improvements are accompanied by an increase in grey matter volume, reported in the left anterior fusiform gyrus/ hippocampus, left precuneus, right hippocampus and right anterior cerebellum
Raschle et al.[43]	20 children	Voxel-based morphometry (VBM)	• Reduced gray matter volumes were reported in the left occipitotemporal, bilateral parietotemporal regions, left fusiform gyrus and right lingual gyrus for pre-reading children with a family-history of dyslexia compared to children without a family-history of dyslexia
Nitzken et al.[44]	30 subjects: 16 dyslexic and 14 control	Analysis of cortex using spherical harmonics (SHs)	• The estimated number of the SHs that approximate the brain shape complexity was used as a discriminant feature to distinguish dyslexic brains from controls
Williams et al.[45]	47 subjects: 16 dyslexic and 31 control	Analysis of cortex using spherical harmonics (SHs)	• The study observed that dyslexic brains exhibit less surface complexity than controls
Evans et al.[40]	118 subjects: 59 dyslexic and 59 control	Voxel-based morphometry (VBM)	• The study reported reduction in the grey matter densities in specific regions based on sex and age
Jednorog et al.[41]	81 subjects: 46 dyslexic and 35 control	Voxel-based morphometry (VBM)	• VBM revealed grey matter volume clusters specific for three studied groups (classified based on the cognitive deficits) including areas of left inferior frontal gyrus, cerebellum, right putamen, and bilateral parietal cortex
Altarelli et al.[46]	29 subjects: 14 dyslexic and 15 control	Analysis of the cortical thickness using Freesurfer software[50]	• The study reported a reduction in thickness in dyslexic children compared with controls in the left hemisphere regions that are responsive to words

connectivity (i.e., the white matter) between different gray matter areas is related to dyslexia. Using VBM, white matter brain regions were identified to be associated with developmental dyslexia. For example, Silani et al.[32] used a VBM method to identify altered white matter density in the left middle and inferior temporal gyri and the left arcuate fasciculus.

Instead of examining the volumetric changes in the white matter densities in the brain, other studies have investigated the shape abnormalities in the white matter in dyslexic brains.[53–56] For example, El-Baz et al.[53–55] quantified the differences between the shape of cerebral white matter (CWM) gyrifications for dyslexic and normal subjects, see Figure 7. The reported results showed

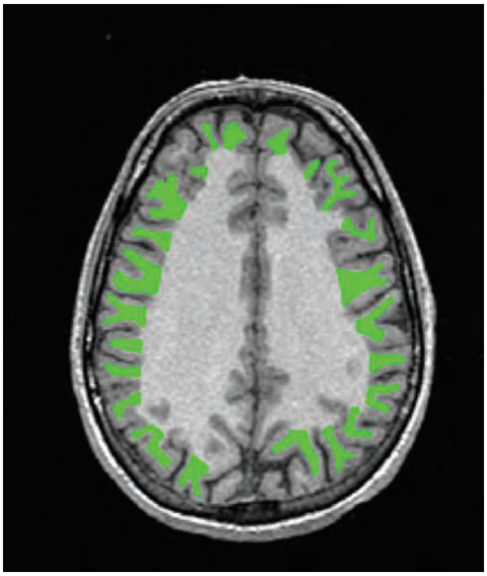


Figure 7. **Extracted CWM gyrifications (green) using the method proposed by El-Baz et al.[53–55]**

statistical significant differences in the reported geometric characteristics of CWM gyrifications between normal and dyslexic subjects. Casanova et al.[56] analyzed the depth of the gyral white matter measured in an MRI series of 15 dyslexic adult men and 11 age-matched comparison subjects. Measurements were based upon the 3D Euclidean distance map inside the segmented cerebral white matter surface.[57–63] Mean gyral white matter depth was 3.05 mm (SD ± 0.30 mm) in dyslexic subjects and 1.63 mm (SD ± 0.15 mm) in the controls. The results added credence to the growing literature suggesting that the attained reading circuit in dyslexia is abnormal. Otherwise, the anatomical substratum (i.e., corticocortical connectivity) underlying this inefficient circuit is normal. Table II summarizes the current MRI-based systems for the detection of dyslexia-associated white matter abnormalities.

Planum Temporale and Cerebellum

Other brain structures, such as the planum temporale and cerebellum, have been studied to investigate their relation to developmental dyslexia.[64–72] The planum temporale is a highly lateralized cortical region located posterior to the auditory cortex within the Sylvian fissure. It is a key anatomical component of Wernicke's area (see Fig. 8), an area which is involved in the understanding of written and spoken language. This structure has shown a significant asymmetry between the two hemispheres of the brain and was found to be larger in the left cerebral hemisphere than the right. Since earlier studies reported a disturbance in the leftward asymmetry in dyslexia,[73–78] several quantitative methods for identifying planum temporale anomalies on the MRI of subjects with developmental dyslexia were developed. For example, Brambati et al.[31] used a VBM analysis to report focal abnormalities in gray matter volume bilaterally in the planum temporale. Larsen et al.[79] analyzed the size and symmetry of the planum temporale using MRI in two groups of normal and dyslexic subjects. The study observed a planum symmetry of around 70% among the dyslexic and around only 30% among the control subjects. Hynd et al.[66] observed that the dyslexic subjects have a smaller left planum temporale, on a study that was performed on 10 dyslexic and 10 normal subjects. Among two groups of 19 dyslexic and 12 control subjects, Leonard et al.[80] used structural MRI to report asymmetry in the left-side temporal bank and the right-side parietal bank within both groups, with the dyslexic brains showing larger asymmetries. The authors explained these exaggerated asymmetries as due to an observed shift of right planar tissue from the temporal to parietal bank in dyslexic individuals. The study also observed a higher incidence of cerebral anomalies bilaterally in dyslexic subjects. More recently, Bloom et al.[81] analyzed the symmetry of the planum temporale to identify possible anomalies in developmental dyslexia. They reported a significantly reduced leftward asymmetry in children with dyslexia.

Although the studies[31, 79–81] showed abnormalities in the asymmetry of the planum temporale in dyslexic individuals, Rumsey et al.[82] analysis for the size and asymmetry of the planum temporale reported different findings. Their study was performed on 16 dyslexic subjects and 14 matched controls that had been previously analyzed using positron emission tomography (PET) during tasks for word recognition and phonological processing.[83] PET analysis showed functional abnormalities (differences in activation

Table II. **Image-based systems for the detection of dyslexia-associated white matter abnormalities using structural MRI. For each study, the number of subjects, the method, and the study findings are reported.**

Study/ref.	Data	Method	Findings
Silani et al.[32]	64 subjects: 32 dyslexic and 2 control	Voxel-based morphometry (VBM)	• Altered white matter density was reported in the left middle and inferior temporal gyri and the left arcuate fasciculus
El-Baz et al.[53–55]	30 subjects: 16 dyslexic and 14 control	Shape analysis of the thickness of CWM gyrifications	• Results reported statistically significant differences in the reported geometric characteristics of CWM gyrifications between normal and dyslexic subjects
Casanova et al.[56]	26 subjects: 15 dyslexic and 11 control	Analysis of the depth of the gyral white matter	• Mean gyral white matter depth was 3.05 mm (SD ± 0.30 mm) in dyslexic subjects and 1.63 mm (SD ± 0.15 mm) in the controls

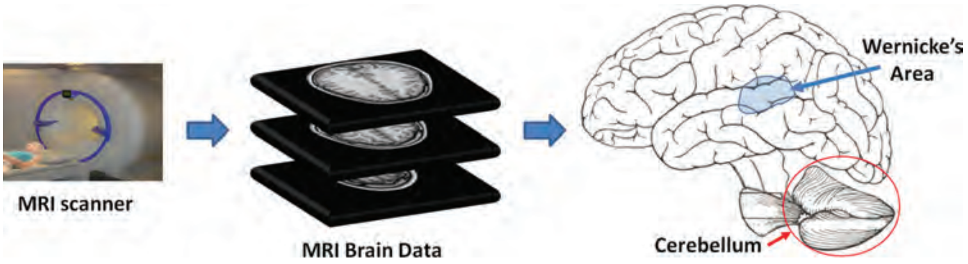


Figure 8. A visualization figure for the brain showing the cerebellum brain structure and the Wernicke's area that the planum temporale forms its heart.

patterns) in temporal and parietal regions in dyslexic individuals, including the posterior portions of the superior temporal gyrus containing the planum temporale.[83] However, their analysis for the size and asymmetry of the planum temporale reported equivalent leftward asymmetries of the planum temporale in the two groups, i.e., the left side is larger than the right side in around 70% to 80% of both groups. They suggested that the anomalous asymmetry of the planum temporale is not strongly associated with dyslexia and did not contribute to the reported functional abnormalities using PET analysis. Correlated with these findings, Robichon et al.[84] reported no morphological difference relative to planum temporale asymmetry between the normal and dyslexic groups.

Other studies attempt to distinguish between dyslexic and control participants using volumetric features extracted from the cerebellum, the superior-most region of the central nervous system (see Fig. 8). Using the VBM analysis, the altered grey matter density was identified in the cerebellum.[29, 30, 33, 38, 71, 85] For example, Brown et al.[30] reported decreased volumes of the gray matter in the cerebellum of dyslexic brains. Kronbichler et al.[29] identified altered grey matter bilaterally in the anterior cerebellum. Pernet et al.[38] reported alterations of the grey matter in the lateral/medial cerebellum. Laycock et al.[71] reported larger volumes of the white matter in both cerebellar hemispheres of the dyslexic group. Based on manual tracing of the cerebellum region, Eckert et al.[86] reported reduced volume of the right anterior lobe of the cerebellum and pars triangularis bilaterally in dyslexic subjects. Using these volumes, 72% of the dyslexic subjects and 88% of the controls were correctly classified. Correlated with these findings, Fernandez et al.[87] also reported reduced volume of the anterior lobe of the cerebellum in dyslexic brains based on manual tracing, which was aided by the cerebellum atlas published by Schmahmann et al.[88] Table III summarizes the current MRI-based systems for the detection of dyslexia-associated abnormalities in the planum temporale and cerebellum. Due to the limited number of these studies, more research should be conducted to provide more accurate findings regarding a possible relation between the planum temporale and cerebellum anomalies to developmental dyslexia.

Corpus Callosum (CC)

The CC is the largest fiber bundle in the brain that is responsible for transferring sensory, motor and cognitive information between homologous regions of the two cerebral hemispheres. Since human reading skills are highly affected by impaired communication between the hemispheres, the detection of CC abnormalities in dyslexia has been an area of research interest. To detect these abnormalities, several studies[89–93] traced the CC from a midsagittal MRI slice either manually[90–92] or with commercial software packages,[93] and the statistical difference analysis has been applied to find out which part in the CC contributes significantly to identifying brains of dyslexic individuals.

Instead of using area metrics that are subject to errors associated with pixel-based measurement, shape-based approaches to detect the shape differences between the CC of normal and dyslexic subjects have been explored. Earlier works for dyslexia detection focused on the 2D analysis of the CC. For example, Plessen et al.[94] computed the mean shape of both dyslexic and normal CCs from the midsagittal slice of the CC and noticed that the CC body length is a discriminatory feature between the dyslexic and normal subjects. To ensure a more accurate quantification of anatomical differences between the CC of dyslexic and control subjects, Casanova et al.[95] and Elnakib et al.[96] applied a 3D analysis method for the CC surface. To ensure a complete 3D analysis, the whole CC surface (traced from all the slices in which the CC appears) is mapped onto a cylinder, in such a way as to accurately compare various CCs of dyslexic and normal individuals.[95–101] Validation on 3D simulated phantoms demonstrated the ability of the method in Refs. [95, 96] to accurately detect the shape variability between two 3D surfaces.[102] Their study[102] reported a generalized increase in size of the CC in dyslexia with a concomitant diminution at its rostral and caudal poles. In addition, they reported significant differences between 14 normal and 16 dyslexic subjects in all four anatomical divisions, i.e., the splenium, rostrum, genu and body of their CCs (see Fig. 9). The 3D analysis of the CC surface resulted in a number of 3D features that can be used to discriminate between dyslexic subjects and controls.[102, 103] In Ref. [103], Elnakib et al. reported significant differences between the CC centerlines (CCL) for 14 normal

Table III. **Image-based systems for the detection of dyslexia-associated abnormalities in the planum temporale and cerebellum using structural MRI. For each study, the number of subjects, the method, and the study findings are reported.**

Study/ref.	Data	Method	Findings
Larsen et al.[79]	28 subjects: 19 dyslexic and 19 control	Analysis of the size and symmetry of the planum temporale	• The results reported a planum symmetry of around 70% among the dyslexic and only around 30% among the control subjects
Hynd et al.[66]	20 subjects: 10 dyslexic and 10 control	Analysis of the size of the planum temporale	• The results reported that the dyslexic subjects have a a smaller left planum temporale than the normal subjects
Leonard et al.[80]	31 subjects: 19 dyslexic and 21 control	Analysis of the size and symmetry of the planum temporale	• Reported asymmetries in the left-side temporal bank and the right-side parietal bank within both groups were observed, with the dyslexic brains showing larger asymmetries
Rumsey et al.[82]	30 subjects: 16 dyslexic and 14 control	Analysis of the size and symmetry of the planum temporale	• Equivalent leftward asymmetries of the planum temporale was reported in around 70% to 80% of both groups
Robichon et al.[84]	30 subjects: 16 dyslexic and 14 control	Analysis of the symmetry of the planum temporale	• No morphological difference was reported relative to planum temporale asymmetry between the normal and dyslexic groups.
Eckert et al.[86]	50 subjects: 32 dyslexic and 18 control	Volumetric measurements of brain regions and cerebellum based on manual tracing	• Reduced volume was observed in the right anterior lobe of the cerebellum and pars triangularis bilaterally of dyslexic brains. Using these volumes, 72% of the dyslexic subjects and 88% of the controls were correctly classified
Eckert et al.[33]	26 subjects: 13 dyslexic and 13 control	Voxel-based morphometry (VBM)	• Altered grey matter density was reported in the cerebellum
Kronbichler et al.[29]	28 subjects: 13 dyslexic and 15 control	Voxel-based morphometry (VBM)	• Altered grey matter density was reported bilaterally in the anterior cerebellum
Laycock et al.[71]	21 subjects: 10 dyslexic and 11 control	Volumetric analysis of the cerebellum brain structure based on manual tracing	• Larger volumes of the white matter were reported in both cerebellar hemispheres of the dyslexic group
Pernet et al.[38]	77 subjects: 38 dyslexic and 39 control	Voxel-based morphometry (VBM)	• Altered grey matter volumes were reported in the lateral/medial cerebellum
Bloom et al.[81]	55 subjects: 29 dyslexic and 26 control	Analysis of the size and symmetry of the planum temporale	• A significant reduction of the leftward asymmetry in children with dyslexia was reported
Fernandez et al.[87]	39 subjects: 23 dyslexic and 16 control	Volumetric analysis of the cerebellum brain structure based on manual tracing	• Reduced volume of the anterior lobe of the cerebellum was observed in dyslexic brains

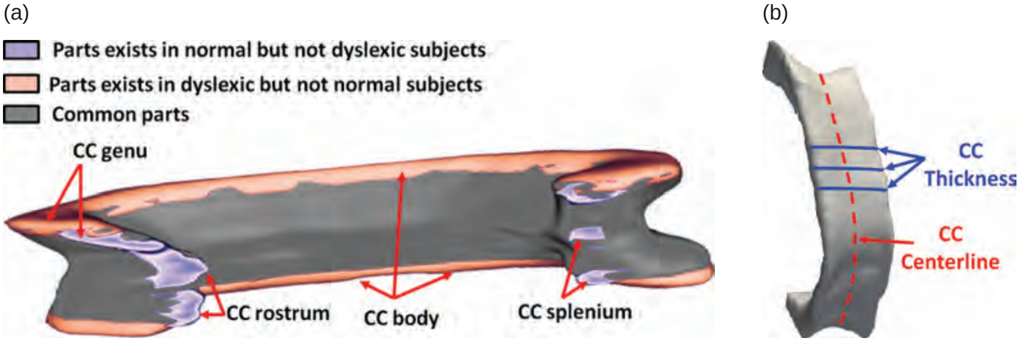


Figure 9. **3D shape analysis of the CC proposed by Elnakib et al.:[102] (a) color-coded anatomical differences between the CC for normal and dyslexic subjects: the common parts (gray), parts that exist in normal subjects and do not exist in dyslexic subjects (lavender), and parts that exist in dyslexic subjects and do not exist in normal subjects (orange), (b) 3D CC features used to classify normal and dyslexic subjects: the centerline length (CLL) and the mean CC thickness (CCT), defined as the mean thickness for each CC cross section perpendicular to the centerline.**

and 16 dyslexic subjects. They extended their work in Ref. [102] and used another feature-the centerline thickness (CCT) defined as the mean thickness for each CC cross section perpendicular to the centerline-to distinguish between normal and dyslexic subjects (see Fig. 9). The combination of the two features (CCL and CCT) showed an increase in the accuracy from 75% (using the CLL alone)-88% (using CCT alone) to 94%. To summarize the current image-based systems for detection of dyslexia-associated abnormalities in CC brain structure, Table IV provides a summary of these systems.

DIFFUSION TENSOR IMAGING (DTI)

DTI is another type of MRI that is based on the measurement of the Brownian motion of water molecules in tissue. DTI is a newly developed MRI technique to study *in vivo* tissue microstructure, e.g., the connectivity between different brain areas. This MRI modality allows the scientist to look at the network of nerve fibers. In addition, the analysis of DTI derives important features of the brain tissue, e.g., FA feature. The latter micro-structural feature reflects how the diffusion within a voxel depends on orientation, i.e., specifies the degree of diffusion directionality. Due to these reasons, DTI has been investigated by neuroscientists to study a number of disorders (e.g., addiction, epilepsy, traumatic brain injury, and various neurodegenerative diseases) and to demonstrate subtle abnormalities in a variety of diseases, (e.g., stroke, multiple sclerosis, dyslexia, and schizophrenia).[104–110] An example of brain nerves' connectivity bundle obtained from a 3D DTI data set is shown in Figure 10.

DTI was used extensively to determine regions related to dyslexia within the white matter.[37, 112–121] Klingberg et al.[112] applied a voxel-based approach based on the SPM software package to spatially smooth and normalize the brains to a common stereotactic space before analyzing the FA values. They reported that the FA scores decrease bilaterally in the temporal-parietal white matter in the subjects with reading difficulties. Correlated with these findings, Beaulieu et al.[122] used DTI to show that the brain connectivity in the white matter, regionally in the left temporo-parietal, is correlated with a wide range of reading abilities in young children (age, 8–12 years).

To avoid the potential influence of spatial smoothing and spatial registration associated with the voxel-based

Table IV. **Image-based systems for the detection of dyslexia-associated CC abnormalities. For each study, the number of subjects, the method, and the study findings are reported.**

Study/ref.	Data	Method	Findings
Hynd et al.[90]	32 subjects: 16 dyslexic and 16 control	Area-based analysis of the CC in the midsagittal MRI brain slice	• The study reported a significantly smaller anterior region of interest (the genu) in the dyslexic children and significant correlations between reading achievement and the region-of-interest measurements for the genu and splenium
Rumsey et al.[91]	40 subjects: 21 dyslexic and 19 control	Area-based analysis of the CC in the midsagittal MRI brain slice	• The study reported a larger area of the posterior third of the CC in dyslexic men than in controls. No differences were reported in the anterior or middle CC
Robichon et al.[92]	28 subjects: 16 dyslexic and 12 control	Area- and morphological-based analysis of the CC in the midsagittal MRI brain slice	• The study reported a more circular and thicker shape of the dyslexics' CC and a larger average midsagittal surface in dyslexic men than in controls, in particular in the isthmus
Fine et al.[93]	68 readers	Area-based analysis of the CC in the midsagittal MRI brain slice	• Results suggested that better readers have larger midsagittal areas at the CC midbody
Plessen et al.[94]	40 subjects: 20 dyslexic and 20 control	Analysis of the CC shape in the midsagittal MRI brain slice	• The study reported a shorter CC length in the dyslexic group, localized in the posterior midbody/isthmus region
Elnakib et al.[103]	40 subjects: 16 dyslexic and 14 controls	3D shape analysis of the CC	• The study reported significant differences between the CC centerlines between normal and dyslexic subjects
Elnakib et al.[96]	40 subjects: 16 dyslexic and 14 controls	3D shape analysis of the CC	• The study reported significant differences between normal and dyslexic subjects in all four anatomical divisions, i.e., splenium, rostrum, genu and body of the CC
Casanova et al.[95]	40 subjects: 16 dyslexic and 14 controls	3D shape analysis of the CC	• The study reported a generalized increase in size of the CC in dyslexia with a concomitant diminution at its rostral and caudal poles
Elnakib et al.[102]	40 subjects: 16 dyslexic and 14 controls	3D shape analysis of the CC	• Combining two features, CCL and CCT, reported an increase in the accuracy of the proposed dyslexia diagnosis system from 75% (using the CLL alone)–88% (using CCT alone) to 94%

Figure 10. Colored streamlines represent likely paths of nerve fiber bundles. This data was extracted from a diffusion imaging data set.

analyses (e.g., with the SPM software), Niogi et al.[114] determined a region of interest either manually or semiautomatically with user-selected seed pixels. They reported significant differences in the FA scores within the left superior corona radiata and the left centrum semiovale comparing children with a reading disability and nonimpaired children. Steinbrink et al.[37] reported a decreased FA in bilateral fronto-temporal and left temporo-parietal white matter regions (inferior and superior longitudinal fasciculus) in dyslexia. A correlation between white matter anisotropy and speed of pseudoword reading was observed. Richards et al.[115] reported alterations of the white matter microstructure in specific bilateral tracts within the frontal lobe, temporal lobe, occipital lobe, and parietal lobe. Carter et al.[116] reported a reduced FA in the left superior longitudinal fasciculus (SLF) and abnormal orientation in the right SLF in dyslexics. Odegard et al.[117] reported correlations between FA values and real word and pseudoword decoding in the left superior corona radiata (positive correlation) and the left posterior CC (negative correlation). Rimrodt et al.[123] reported reduced FA values in the left inferior frontal gyrus and left temporoparietal white matter of dyslexic brains. Van dermosten et al.[118] reported a reduced FA in the left arcuate fasciculus of adults with dyslexia. In an extension of this work, Vandermosten et al.[119] reported a reduction in the white matter lateralization in both the posterior superior temporal gyrus and the arcuate fasciculus in the dyslexic readers. Hasan et al.[120] studied the utility of regional DTI measurements of the CC in understanding the neurobiology of reading disorders in a group of 50 childen: 24 dyslexics, 15 readers with comprehension or fluency problems, and 11 controls. They analyzed the diffusion attributes in the midsagittal cross-sectional CC subregions using DTI. The results reported a significant correlation of the callosal microstructural attributes, such as the mean diffusivity of the posterior middle sector of the CC, with measures of word reading and reading comprehension. In addition, reading group differences in FA, mean diffusivity and radial diffusivity were observed in the posterior CC. Table V summarizes the current DTI-based systems for the detection of dyslexia-associated white matter microstructure abnormalities.

FUNCTIONAL MRI

Functional magnetic resonance imaging (fMRI) is a noninvasive MRI technique that is used to study the activated area of the brain after certain stimuli and to map changes of brain hemodynamics that correspond to mental operations. The technique has the ability to observe which structures participate in specific mental tasks.[124] Functional MRI acquires two images, one while the brain is in the resting state followed by another one after the brain has been stimulated in some way. The areas of brain activation are determined as any regions which are different between the two scans. Functional MRI allows radiologists to better understand brain organization and has the advantage of providing in-depth details of how the brain works.

In the literature, fMRI has played an important role in understanding the pathophysiology of dyslexia and analyzing the neural brain systems for reading.[125–130] It has been used extensively to analyze the activation areas of the brain associated with the reading process within groups of normal and dyslexic subjects. Rimrodt et al.[131] used fMRI to observe brain activation associated with sentence comprehension (SC) and word recognition (WR) in two groups of 14 dyslexic subjects and 15 controls. Activation areas associated with the SC-WR contrast were reported in left inferior frontal and extrastriatal regions. The dyslexic group showed more activation than controls in the left middle/superior temporal gyri (areas associated with linguistic processing), bilateral insula, right cingulate gyrus, right superior frontal gyrus, and right parietal lobe (areas associated with attention and response selection). Baillieux et al.[132] used fMRI to analyze the activation patterns of 15 dyslexic children and 7 matched control subjects during a semantic association task. The activation patterns showed significant differences in cerebral and cerebellar activation between the dyslexic and the control groups. Focal activation patterns were found in the control group bilaterally in the frontal and parietal lobes and the posterior regions of the two cerebellar hemispheres. In contrast, diffuse activation was reported on cerebral and cerebellar regions of dyslexic subjects. The authors suggested the association between dyslexia and deficits of information processing and transfer within the cerebellar cortex. Reilhac et al.[133] used fMRI to investigate functional abnormalities in dyslexic children with visual attention span disorder during a letter-string comparison task. A lower accuracy of detecting letter identity substitutions within strings was reported in dyslexic subjects. Compared to the control group, under-activation was detected in the left superior parietal lobules and the left

Table V. Image-based systems for the detection of dyslexia-associated white matter microstructure abnormalities using DTI. For each study, the number of subjects, the method, and the study findings are reported.

Study/ref.	Data	Method	Findings
Klingberg et al.[112]	17 subjects: 6 dyslexic and 11 control	A voxel-based approach based on the SPM software to define the regions and statistical analysis to analyze FA values	- The study reported reduced FA scores bilaterally in the temporal-parietal white matter in the subjects with reading difficulties
Beaulieu et al.[122]	32 subjects	A voxel-based approach based on the SPM software to define the regions and statistical analysis to analyze FA values	- The study reported that the brain connectivity in the white matter, regionally in the left temporo-parietal, is correlated with a wide range of reading abilities in young children
Niogi et al.[114]	31 subjects: 11 dyslexic and 20 control	Manual or semiautomated determination of the region of interest to analyze the FA values	- They reported significant differences in the FA scores within the left superior corona radiata and the left centrum semioval between children with a reading disability and non-impaired children
Steinbrink et al.[37]	16 subjects: 8 dyslexic and 8 control	Analysis of DTI data to examine white matter microstructure	- DTI reported reduced FA scores in the dyslexic group in bilateral fronto-temporal and left temporo-parietal white matter regions (inferior and superior longitudinal fasciculus)
Richards et al.[115]	21 subjects: 14 dyslexic and 7 control	Voxel-wise statistical analysis of the fractional anisotropy data using tract-based spatial statistics	- Alterations of the white matter microstructure were reported in the dyslexic group in specific bilateral tracts within the frontal lobe, temporal lobe, occipital lobe, and parietal lobe
Carter et al.[116]	13 subjects: 7 dyslexic and 6 control	Analysis of DTI data to examine white matter microstructure	- A reduced FA score was reported in the dyslexic group in the left superior longitudinal fasciculus (SLF) and an abnormal orientation was found in the dyslexic group in the right SLF
Odegard et al.[117]	17 subjects: 10 dyslexic and 7 control	Voxel-wise statistical analysis of the fractional anisotropy data using tract-based spatial statistics	- Correlations between FA values and real word and pseudoword decoding were reported in the left superior corona radiata (positive correlation) and the left posterior corpus callosum (negative correlation)
Rimrodt et al.[123]	31 subjects: 14 dyslexic and 17 control	Semi-automated analysis of DTI data to examine white matter microstructure	- Reduced FA scores were reported in the dyslexic subjects in left inferior frontal gyrus and left temporo-parietal white matter
Hasan et al.[120]	50 children: 24 dyslexic, 15 readers with comprehension or fluency problems, and 11 controls	Diffusion analysis of midsagittal crosssectional CC subregions using DTI	- Reading group differences in FA, mean diffusivity, and radial diffusivity were observed in the posterior CC
Vandermosten et al.[118, 119]	40 subjects: 20 dyslexic and 20 control	Analysis of DTI data to examine white matter microstructure	- Reduced white matter lateralization was reported in the posterior superior temporal gyrus[119] and the arcuate fasciculus[118, 119] of the dyslexic group

ventral occipito-temporal area of dyslexic subjects, suggesting that these regions may participate in letter string processing. Olulade et al.[134] analyzed fMRI activation patterns of 9 reading-disabled and 12 control subjects during the analysis of complex spatial material unrelated to the reading of text. To perform that, two spatial problem solving tasks were tested: a word reading-rhyming task and a spatial visualization-rotation task. Reduced activation was observed in bilateral occipital, parietal and middle frontal regions in the reading-disabled group during both spatial tasks. The authors suggested that the underlying neural abnormality in dyslexic brains may affect non-related reading processes. In addition, they suggested that this abnormality may be reflected on other left hemisphere brain areas that are not associated with text reading.

In addition, fMRI has been used extensively to analyze brain functionality in dyslexia during phonological processing.[135–141] For example, Shaywitz et al.[135] analyzed fMRI activation patterns of 26 dyslexic subjects and 23 control subjects during a phonological analysis task. Under-activation was observed in Wernicke's area, the angular gyrus, and striate cortex and over-activation was observed in the inferior frontal gyrus, suggesting a neural deficit in dyslexia. Shaywitz et al.[136] used fMRI to analyze the activation patterns of dyslexic children during tasks that required phonologic analysis (i.e., during pseudoword and real-word reading tasks). The study was conducted on 70 dyslexic cildren and 74 controls. The dyslexic subjects reported deficits in the posterior brain regions, including regions in the parietotemporal and occipitotemporal sites. The activation magnitude in the left occipitotemporal region was positively correlated with the reading skill. In addition, younger dyslexic children exhibited lower activation in the left and right inferior frontal lobe compared with older dyslexic children. The authors suggested that dyslexic children have deficits in the neural systems involved in reading that become evident at a young age. Georgiewa et al.[137] analyzed the activation patterns of 9 dyslexic and 8 control children during nonoral reading of German words. Compared to the control group, fMRI reported hyper-activation in the left inferior frontal gyrus in the dyslexic group suggestive of abnormalities in phonological processing. The control subjects exhibited activation in the left middle temporal gyrus area, whereas this area showed disturbed activity in dyslexics. Groth et al.[138] used fMRI to study the auditory temporal and phonological processing in dyslexic individuals using a German vowel length discrimination task. Dyslexic subjects performed worse than controls in response to temporal processing, whereas they did not differ in response to phonological processing. The study suggested that dyslexia is associated with impairments in temporal processing. The group extended their study in Ref. [139] and showed that the dyslexic subjects, who performed low in response to temporal processing, showed decreased activation of the insular cortices and the left inferior frontal gyrus. These results suggested a neural basis for the deficits in the temporal auditory processing for dyslexic subjects. Díaz et al.[140] analyzed fMRI activation patterns of 14 dyslexic subjects and 14 matched controls during a phonological task (attending to speech sound changes) and a speaker task (attending to changes in voice characteristics). For both tasks, the dyslexic subjects exhibited abnormal activation of the medial geniculate body of the auditory sensory thalamus. In addition, this activity was correlated with reading scores, suggesting that the dysfunction of the auditory thalamus may participate in dyslexia. Kovelman et al.[141] analyzed fMRI activation patterns of 12 dyslexic, 12 age-matched control children, and 10 Kindergarten controls, who were matched to dyslexic children based on standardized tests of phonological awareness. During an auditory word-rhyming task, both control groups, but not the dyslexic, showed activation in the left dorsolateral prefrontal cortex, suggesting that phonological awareness may depend on the proper function of this region.

Moreover, fMRI has been used to investigate the neural integration of letters and speech in the brains of dyslexic individuals.[1, 142] Blau et al.[1] analyzed fMRI activation patterns of 13 dyslexic and 13 control subjects during four conditions of either reading letters or understanding speech sounds: visual, auditory, congruent audiovisual speech stimuli, and incongruent audiovisual speech stimuli. The study revealed under-activation of the superior temporal cortex in the dyslexic group when integrating letter and speech sounds, suggesting a deficit in the neural integration of letters and speech in dyslexic brains. The group extended their work in Ref. [142] on 18 dyslexic children and 16 control children to study letter-speech sound integration in dyslexia. The study reported reduced neural integration of letters and speech sounds in the planum temporale/Heschl sulcus and the superior temporal sulcus in dyslexic subjects. The authors suggested that letter-speech sound integration contributes to learning to read but may be poorly developed in dyslexia.

Investigation of the pathophysiology of dyslexic brains using fMRI has been the focus of several research studies.[143–145] Demb et al.[144] used fMRI to analyze the pathophysiology of dyslexic brains in an experiment using visual stimuli. The primary visual cortex and extrastriatal areas showed reduced activations in dyslexic subjects, suggesting a deficit in the magnocellular pathway in the dyslexic brains. In Ref. [143], Eden et al. used fMRI to study visual motion processing on 6 dyslexic subjects and 8 controls. During the presentation of stationary patterns, both groups showed same activation in the extrastriatal cortex and V5/MT area-a part of the magnocellular visual subsystem located in the extrastriatal visual area that has been previously characterized for visual motion processing.[146] During the presentation of moving stimuli, the V5/MT area was activated in the control but not the dyslexic group. Peyrin et al.[145] investigated neurobiological evidence from fMRI for the reported dissociation between phonological and visual attention span disorders in dyslexic children.[147] The study analyzed the activation patterns of two dyslexic subjects: one with a phonological disorder but preserved visual attention span abilities and the second with the reverse profile. fMRI reported a decreased activation in the left inferior frontal gyrus of the first subject during a phonological rhyme judgment task, whereas the second subject exhibited a normal level of activation in this region. In contrast, a decreased activation of the parietal lobules was reported in the second subject during a visual categorization task, whereas these regions were normally activated in the first subject. In spite of the limited number of the tested subjects, the study provided insights about a possible relation between distinct cognitive impairments and distinct brain dysfunctions in dyslexia.

The brain activation patterns in dyslexia have also been investigated during working memory tasks.[148–150] Wolf et al.[148] used fMRI to investigate the functional neuroanatomy underlying cognitive dysfunction in dyslexia. To perform this task, the study analyzed the activation pattern of 12 dyslexic subjects and 13 controls during a verbal working memory task. The dyslexic subjects were slower than the controls. In addition, they were less accurate as the demand of the working memory increased. During working memory subprocesses, the authors identified abnormal connectivity patterns in the dyslexic subjects in two brain networks: a “phonological” network (associated with the recognition of verbal stimuli) and an “executive” network (associated with the accuracy of the working memory task and the number of errors during a spelling test). The dyslexic subjects exhibited an increased connectivity pattern within the “phonological” network in the left prefrontal and inferior parietal regions. Within the "executive" network, the dyslexic subjects showed an increased functional connectivity in the left angular gyrus, the right superior parietal cortex, the left inferior frontal gyrus, the left hippocampal gyrus, and the right thalamus whereas they exhibited a decreased functional connectivity in the bilateral dorsolateral prefrontal cortex, the left cuneus, the left insula, the right inferior parietal lobule, and the right precuneus. The authors suggested that the working memory dysfunction in dyslexia may be due to an abnormal functional connectivity in dissociable brain networks that are related to "phonological" and "executive" working memory subprocesses. Beneventi et al.[149] investigated the brain activation patterns of the dyslexic subjects associated with phonological storage and rehearsal of serial order in working memory using two sequential verbal working memory tasks: a single letter probe task (judge if the current single letter probe exist in a prior sequence of six letters) and a sequence probe task (judge if the serial order of the current sequence of six letters probe match the prior sequence). In the single letter probe task, the dyslexic group showed reduced activation in the left precentral gyrus (BA6) compared to the control group. In the sequence probe task, the dyslexic group showed reduced activation in the prefrontal cortex and the superior parietal cortex (BA7) compared to the control subjects. Another study by Beneventi et al.[150] analyzed fMRI activation patterns of 11 dyslexic subjects and 13 controls during a working memory task. Reduced activation was observed in the left superior parietal lobule and the right inferior prefrontal gyrus in the dyslexic group. As the working memory load increased, the control subjects, but not the dyslexic subjects, exhibited increased activation in the working memory area, suggesting abnormal deficit in the working memory in dyslexic brains.

Other fMRI studies have investigated the functional brain connectivity in specific brain regions in response to different processing tasks.[151–153] For example, Pugh et al.[151] used fMRI to investigate the functional connectivity in dyslexic brains around the angular gyrus in the left hemisphere during print tasks that require phonological assembly. The study was conducted on 29 dyslexic and 32 control subjects. The functional connectivity exhibited strong patterns in both groups in print tasks that do not require phonological assembly. In tasks that depend on assembly, disruption in functional connectivity was observed in the left hemisphere in the dyslexic group, suggesting a neural deficit in dyslexia associated with phonological-processing. Quaglino et al.[152] used fMRI to investigate the functional connectivity patterns between the supramarginal cortex (BA 40; BA: Brodmann area), fusiform cortex (BA 37) and inferior frontal cortex (BA 44/45) areas of the left hemisphere in dyslexic subjects during a pseudoword reading task. This study was performed on three groups: 6 dyslexic subjects, 6 agematched control subjects, and 6 reading level-matched control subjects. The dyslexic group showed no connectivity between BA 40 and BA 44/45, whereas both the dyslexic group and the reading levelmatched group showed a strong connectivity between BA 37 and BA 44/45. Van der Mark et al.[153] used fMRI to analyze the connectivity of the visual word form area (VWFA),[154] within the larger left occipitotemporal cortex, to its neighboring language regions. The study analyzed the activation patterns in 18 dyslexic children and 24 matched controls during a continuous reading task. In the control group, the VWFA area was functionally connected to the left frontal and parietal language areas, but not connected to adjacent posterior and anterior regions. In contrast, the dyslexic group showed functional disconnectivities between the VWFA area and left inferior frontal and left inferior parietal language areas. The authors suggested that the deficits in the functional connectivity between the VWFA area and major language areas may lead to problems in orthographic and phonological processing of visual word forms.

Multiple fMRI studies have analyzed the functional brain activation patterns of the brain regions in response to different processing tasks.[155–159] For example, Temple et al.[155, 158] analyzed the brain activation patterns of dyslexic subjects in response to rapidly changing, relative to slowly changing nonlinguistic acoustic stimuli (to mimic the spectro-temporal structure of consonant-vowel-consonant speech syllables). While the normal group showed left prefrontal activity for rapid compared to slow transitions nonlinguistic acoustic stimuli, the dyslexic group showed no differences in their left frontal response. This group extended their work in Gaab et al. study[158] and observed, after eight weeks of remediation, left prefrontal cortex activation in the dyslexic group for rapid relative to slow transitions as well as an enhancement in their reading skills. Backes et al.[156] observed the fMRI activation patterns of the dyslexic brains in response to varying tasks that involve visuospatial, orthographic, phonologic, and semantic processing demands. The left extrastriate exhibited enhanced activation during all tasks in the dyslexic subjects. The right prefrontal cortex was activated during both the orthographic processing and the visuospatial tasks in the dyslexic subjects. The temporal and the prefrontal cortex showed reduced activation in the dyslexic group than the normal group during the phonologic processing task. The authors suggested that the dyslexic subjects tend to process the different brain tasks using the visuospatial processing brain areas instead of the normal language processing areas, due to a failure in their language processing brain areas in processing the brain tasks. Ruff et al.[160] studied the activation patterns of the dyslexic subjects using a stimuli from a phonetic continuum between two natural syllables during a pseudo-passive listening task which does not imply voluntary categorical judgment. Regions in the left angular gyrus, the right inferior frontal gyrus, and the right superior cingulate cortex showed activation in the control group motivated by the categorical deviant stimuli, whereas these regions were not activated in the dyslexic group. Their study reported activation in the dyslexic group for acoustic but not phonetic changes in stimuli. Karni et al.[157] used blood-(de)oxygenation-level-dependent (BOLD) fMRI to investigate the functional brain activation patterns of dyslexic subjects during three reading and script processing tasks (with slow (routine) vs. fast word reading rates): sentences (plausibility judgment), single words (concrete/abstract judgment), and nonwords (homophonic judgment). For fast reading rates, the comprehension and accuracy were impaired in both the control and dyslexic groups. For the sentences and single words processing tasks, the control group exhibited higher activations in the visual areas associated with fast reading rate, whereas it show no differences with the dyslexic group for the slow reading rate. For the slow non-words processing task, the Brocas area and operculum were activated in the dyslexic group, where as the visual processing areas (extra-striate cortex) were activated in the control group. Heim et al.[159] observed the activation patterns of dyslexic subjects during different tasks: reading ability, auditory discrimination, phonological awareness, visuo-magnocellular motion perception, and attention shifting (a magnocellular function). During motion detection and auditory discrimination, the dyslexic group showed reduced activation in the visual cortex and the auditory cortex, respectively. During magnocellular tasks, they exhibited increased right frontal activation in areas 44 and 45. During phonological decisions, they had reduced activation than the control group in left areas 44 and 45.

Several other studies have investigated the functional activation of dyslexic subjects before and after treatment using fMRI.[161–165] For example, Temple et al.[162] analyzed the functional activation of 20 dyslexic subjects and 12 normal subjects during phonological processing before and after a treatment program that was based on auditory processing and oral language training. In association with behavioral improvement in the oral language and reading performance in the dyslexic group after the treatment, fMRI revealed improved activation in the left temporo-parietal cortex and left inferior frontal gyrus such that it approximated the normal group. In addition, the right-hemisphere frontal and temporal regions and the anterior cingulate gyrus exhibited increased activation in the dyslexic group. The study reported a positive correlation between the ability of the oral language with the magnitude of activation in the left temporo-parietal cortex. Aylward et al.[163] analyzed the functional activation of 10 dyslexic subjects and 11 normal subjects before and after 28 hours of comprehensive reading instruction. The study analyzed the brain functionality during two different reading tasks: a phoneme mapping task (i.e., mapping sounds to letters) and a morpheme mapping task (i.e., understanding the relation between suffixed words and their roots). Prior to instructional treatment, the left middle and inferior frontal gyri, right superior frontal gyrus, left middle and inferior temporal gyri, and bilateral superior parietal regions showed reduced activation in the dyslexic subjects during the phoneme mapping task. In addition, left middle frontal gyrus, right superior parietal, and fusiform/occipital region exhibited lower activation in the dyslexic subjects during the initial morpheme mapping task. After instructional treatment, the reading scores of the dyslexic subjects showed an improvement that was associated with an increase in the brain activation during both tasks, whereas a decrease in the brain activation was observed in the normal group during both tasks in a way that they approximated the dyslexics' activation. The authors suggested that comprehensive reading instruction can lead to behavioral gains that may be evident on the brain activation patterns during reading tasks. Eden et al.[166] investigated the brain activation patterns during a phonological manipulation task before and after a behavioral intervention. After phonologically targeted training, the dyslexic group exhibited an increased activation in the left-hemisphere regions that were engaged by the control group. This increased activation is associated with a compensatory activity in the right perisylvian cortex as well as an improvement in the reading performance of the dyslexic group. Richards et al.[164] observed the fMRI activation patterns associated with a set of word-form tasks after an orthographic and morphological spelling treatment. After orthographic treatment, dyslexic subjects showed treatment-specific response in right inferior frontal gyrus and right posterior parietal gyrus. Another study, by Richards et al.[165] investigated the functional activation of dyslexic subjects before and after treatment using fMRI during a phoneme mapping task. After a three-week instructional treatment program, the regions that exhibited abnormal functional activation in the dyslexic subjects (i.e., in the left frontal gyrus) showed no differences between the dyslexic and normal groups. The authors suggested that instructional treatment may normalize the abnormal functional activation. Zhang et al.[167] observed the brain activation during a visual task: observing the change of an arrows direction in a complex, relative to a simple, visual background. The dyslexic group showed a reduced activation in occipital visual areas associated with visual perception, and an increased activation in frontal and parietal regions associated with visual attention. The authors suggested an abnormal organization of the dyslexic brains when processing tasks of visual shape extraction that does not involve reading.

Other fMRI studies investigate abnormal neural systems of dyslexic brains in non-English readers.[168–170] For example, Wimmer et al.[168] investigated dyslexia among German readers using fMRI. During lexical route processes, under-activation was reported in the left ventral occipitotemporal region of the dyslexic subjects. During sublexical route processes, under-activation was reported

Table VI. **Image-based systems for the detection of dyslexia-associated functional abnormalities using fMRI. For each study, the number of subjects, the method, and the study findings are reported.**

Study/ref.	Data	Method	Findings
Eden et al.[143]	14 subjects: 8 dyslexic and 6 control	Analysis of fMRI activation during visual motion processing	• During the presentation of stationary patterns, both groups show same activation in the extrastriatal cortex and V5/MT area. During the presentation of moving stimuli, the V5/MT area was activated in the control but not the dyslexic group
Demb et al.[144]	10 subjects: 5 dyslexic and 5 control	Analysis of fMRI activation using a visual stimuli experiment	• The primary visual cortex and areas in the extrastriatal cortex showed reduced activations in dyslexic subjects
Shaywitz et al.[135]	49 subjects: 26 dyslexic and 23 control	Analysis of fMRI activation during a phonological analysis task	• Under-activations were observed in Wernicke's area, the angular gyrus, and striate cortex. Over-activation was observed in the inferior frontal gyrus
Pugh et al.[151]	61 subjects: 29 dyslexic and 32 control	Analysis of functional connectivity around the angular gyrus in the left hemisphere during print tasks that require phonological assembly	• The functional connectivity exhibited strong patterns in both groups in print tasks that do not require phonological assembly. In tasks that depend on assembly, disruption in functional connectivity was observed in the left hemisphere in the dyslexic group
Temple et al.[155]	18 subjects: 8 dyslexic and 10 control	Analysis of functional activation patterns in response to rapidly changing, relative to slowly changing, nonlinguistic acoustic stimuli	• The normal group showed left prefrontal activity in response to rapidly changing, relative to slowly changing, nonlinguistic acoustic stimuli, whereas the dyslexic group showed no differences in the left frontal response
Seki et al.[169]	10 subjects: 5 dyslexic and 5 control	Analysis of fMRI activation of dyslexic Japanese during a reading task of sentences constructed from Japanese phonograms (kana)	• The left middle temporal gyrus was significantly activated in the control subjects but was less activated in the dyslexic subjects. Other activated regions were detected in particular dyslexic subjects
Georgiewa et al.[137]	17 subjects: 9 dyslexic and 8 control	Analysis of fMRI activation during non-oral reading of German words	• Compared to the control group, fMRI reported hyper-activation in the left inferior frontal gyrus in dyslexic group. The control subjects exhibited activation in the left middle temporal gyrus area, whereas this area showed disturbance activity in the dyslexic subjects
Shaywitz et al.[136]	144 subjects: 70 dyslexic and 74 control	Analysis of fMRI cerebral and cerebellar activation during tasks that required phonologic analysis	• The dyslexic subjects reported deficits in the posterior brain regions. The activation magnitude in the left occipitotemporal region was positively correlated with the reading skill. Younger dyslexic children exhibited lower activation in the left and right inferior frontal compared with older dyslexic children
Backes et al.[156]	16 subjects: 8 dyslexic and 8 control	Analysis of fMRI activation patterns during tasks that involve visuospatial, orthographic, phonologic, and semantic processing demands	• The right prefrontal cortex was activated during both orthographic processing and the visuospatial tasks in the dyslexic subjects. The temporal and the prefrontal cortex showed reduced activation in the dyslexic group than the normal group during phonologic processing task
Ruff et al.[160]	26 subjects: 12 dyslexic and 14 control	Analysis of fMRI activation patterns during during a pseudo-passive listening task which does not imply voluntary categorical judgment	• Regions in the left angular gyrus, the right inferior frontal gyrus, and the right superior cingulate cortex showed activation in the control group motivated by the categorical deviant stimuli, whereas these regions were not activated in the dyslexic group. Their study reported activation in the dyslexic group for acoustic but not phonetic changes in stimuli
Temple et al.[162]	32 subjects: 20 dyslexic and 12 control	Analysis of fMRI activation before and after instructional treatment using a phonological processing task	• fMRI, after treatment, revealed an improved activation in the left temporoparietal cortex and left inferior frontal gyrus such that it get close to the normal group. In addition, the right-hemisphere frontal and temporal regions and the anterior cingulate gyrus exhibited an increased activation in the dyslexic group. The study reported a positive correlation between the ability of the oral language with the magnitude of activation in the left temporo-parietal cortex
Aylward et al.[163]	21 subjects: 10 dyslexic and 11 control	Analysis of fMRI activation before and after 28 hours of instructional treatment using two different reading tasks: a phoneme mapping task and a morpheme mapping tasks	• After instructional treatment, the brain activation during both tasks increased in the dyslexic group and decreased in the normal group such that they get close to each other

Table VI. Continued.

Study/ref.	Data	Method	Findings
Eden et al.[166]	38 subjects: 19 dyslexic and 19 control	Analysis of fMRI activation during a phonological manipulation task before and after a behavioral intervention	• After phonologically targeted training, the dyslexic group exhibited an increased activation in the left-hemisphere regions that were engaged by the control group. This increased activation is associated with a compensatory activity in the right perisylvian cortex as well as an improvement in the reading performance of the dyslexic group
Karni et al.[157]	16 subjects: 8 dyslexic and 8 control	Analysis of fMRI activation during reading and script processing tasks with slow (routine) versus fast word reading rates	• For fast reading rates, the comprehension and accuracy were impaired in both the control and dyslexic groups. For the sentences and single words processing tasks, the control group exhibited higher activations in the visual areas associated with fast reading rate, where as it show no differences with the dyslexic group for the slow reading rate. For the slow non-words processing task, the Brocas area and operculum were activated in the dyslexic group, whereas the visual processing areas (extra-striate cortex) was activated in the control group
Richards et al.[164]	39 subjects: 18 dyslexic and 21 control	Analysis of fMRI activation before and after treatment using a set of word-form tasks	• After orthographic treatment, dyslexic subjects showed treatment-specific response in right inferior frontal gyrus and right posterior parietal gyrus
Gaab et al.[158]	45 subjects: 22 dyslexic and 23 control	Analysis of functional activation patterns in response to rapidly changing, relative to slowly changing, nonlinguistic acoustic stimuli	• After eight weeks of remediation, left prefrontal cortex activation was observed in the dyslexic group for rapid relative to slow transitions
Quaglino et al.[152]	18 subjects: 6 dyslexic and 12 control	Analysis of the functional connectivity between the BA 40, BA 37, and BA 44/45 areas of the left hemisphere during a pseudoword reading task	• The dyslexic group showed no connectivity between BA 40 and BA 44/45, whereas both the dyslexic group and the reading level-matched group showed a strong connectivity between BA 37 and BA 44/45
Richards et al.[165]	39 subjects: 18 dyslexic and 21 control	Analysis of fMRI activation during a phoneme mapping task before and after a 3-week instructional treatment program	• After treatment, the regions of abnormal functional activation in the dyslexic subjects (i.e., in the left frontal gyrus) showed no difference between the dyslexic and normal groups
Siok et al.[172]	32 subjects: 16 dyslexic and 16 control	Analysis of fMRI activations patterns of the cortical brain regions of the Chinese dyslexic readers during a rhyme judgment task	• Reduced gray matter volume as well as reduced functional activation were reported in a left middle frontal gyrus region for the dyslexic group in comparable to the control group
Blau et al.[1]	39 subjects: 18 dyslexic and 21 control	Analysis of fMRI activation during four conditions for reading: visual, auditory, audiovisual congruent, and audiovisual incongruent	• Under-activation was observed in the superior temporal cortex in the dyslexic group when integrating letter and speech sounds
Rimrodt et al.[131]	29 subjects: 14 dyslexic and 15 control	Analysis of fMRI activation areas of the brain during a sentence comprehension and a word recognition tasks	• Dyslexic group showed more activation than controls in the left middle/superior temporal gyri (areas associated with linguistic processing), and in the bilateral insula, right cingulate gyrus, right superior frontal gyrus, and right parietal lobe (areas associated with attention and response selection)
Beneventi et al.[149]	24 subjects: 11 dyslexic and 13 control	Analysis of fMRI activation associated with phonological storage and rehearsal of serial order in working memory using sequential verbal working memory tasks	• In the letter probe task, the dyslexic group showed reduced activation in the left precentral gyrus (BA6) compared to control group. In the sequence probe task, the dyslexic group showed reduced activation in the prefrontal cortex and the superior parietal cortex (BA7) compared to the control subjects
Baillieux et al.[132]	22 subjects: 15 dyslexic and 7 control	Analysis of fMRI cerebral and cerebellar activation during a semantic association task	• Diffused activations were reported on the cerebral and cerebellar regions in the dyslexic subjects, whereas these areas showed focal activation in the controls
Wimmer et al.[168]	39 subjects: 20 dyslexic and 19 control	Analysis of fMRI activation among dyslexic German readers during lexical and sublexical route processes	• The authors reported a different neural organization of reading processes in German dyslexic readers than the reported one[171] for English readers

Table VI. **Continued.**

Study/ref.	Data	Method	Findings
Wolf et al.[148]	25 subjects: 12 dyslexic and 13 control	Analysis of fMRI activation during verbal working memory task	• The authors identified abnormal connectivity patterns in the dyslexic subjects in two brain networks: a “phonological” (associated with the recognition of verbal stimuli) network and an “executive” network (associated with the accuracy of the working memory task and the number of errors during a spelling test)
Beneventi et al.[150]	24 subjects: 11 dyslexic and 13 control	Analysis of fMRI activation during a working memory task	• Reduced activations were observed in the left superior parietal lobule and the right inferior prefrontal gyrus in the dyslexic group. As the working memory load increased, the control, but not the dyslexic subjects, exhibited increased activation in the working memory area
Blau et al.[142]	34 subjects: 18 dyslexic and 16 control	Analysis of fMRI activation during four conditions for reading: visual, auditory, audiovisual congruent, and audiovisual incongruent	• Reduced neural integration of letters and speech sounds was reported in the planum temporale/Heschl sulcus and the superior temporal sulcus in the dyslexic subjects
Van der Mark et al.[153]	42 subjects: 18 dyslexic and 24 control	Analysis of fMRI connectivity around the visual word form area (VWFA)[154] during a continuous reading task	• Deficits in the functional connectivity between the VWFA area and major language areas were reported in the dyslexic group
Groth et al.[138]	40 subjects: 20 dyslexic and 20 control	Analysis of fMRI activation areas of the brain during auditory temporal and phonological processing	• Dyslexic subjects performed worse than controls in response to temporal processing, whereas they did not differ in response to the phonological processing
Steinbrink et al.[139]	40 subjects: 20 dyslexic and 20 control	Analysis of fMRI activation areas of the brain during auditory temporal and phonological processing	• In response to temporal processing, dyslexic subjects performed low and showed decreased activation of the insular cortices and the left inferior frontal gyrus
Peyrin et al.[145]	2 dyslexic subjects	Analysis of fMRI activation during two tasks: a phonological rhyme judgement task and a visual categorization task	• The fMRI of the two dyslexic children reported a dissociation between phonological and visual attention span disorders
Reilhac et al.[133]	24 subjects: 12 dyslexic and 12 control	Analysis of fMRI activation of dyslexic children with visual attention span disorder during a letter-string comparison task	• A lower accuracy of detecting letter identity substitutions within strings was reported in the dyslexic subjects. Under-activations were detected in the left superior parietal lobules and the left ventral occipitotemporal in the dyslexic subjects
Díaz et al.[140]	28 subjects: 14 dyslexic and 14 control	Analysis of fMRI activation during a phonological task	• The dyslexic subject exhibited an abnormal activation in the medial geniculate body of the auditory sensory thalamus
Olulade et al.[134]	21 subjects: 9 dyslexic and 12 control	Analysis of fMRI activation during two spatial problem solving tasks: a word reading-rhyming task and a spatial visualization-rotation task	• Abnormal functional neurology was reported during spatial problem solving tasks
Kovelman et al.[141]	24 subjects: 12 dyslexic and 12 control	Analysis of fMRI activation during an auditory word-rhyming task	• Control subjects, but not the dyslexic, showed activations in the left dorsolateral prefrontal cortex
Zhang et al.[167]	24 subjects: 11 dyslexic and 13 control	Analysis of fMRI activation during visual shape extraction	• The dyslexic group showed a reduced activation in occipital visual areas associated with visual perception, and an increased activation in frontal and parietal regions associated with visual attention
Kita et al.[170]	29 subjects: 14 dyslexic and 45 control	Analysis of fMRI activation during a phonological manipulation task	• The phonological task activated areas in the left inferior and middle frontal gyrus, left superior temporal gyrus, and bilateral basal ganglia. A hyperactivity and hypo-activity were observed in the basal ganglia and the left superior temporal gyrus, respectively, in the dyslexic group

in the left inferior parietal region and in the left inferior frontal region in the dyslexic subjects. Overactivation was reported in visual occipital regions, premotor/motor cortex, and subcortical caudate and putamen in the dyslexic subjects. Both the dyslexic and the control subjects exhibited no activations in the posterior temporal regions, which have shown abnormalities in fMRI studies on English readers.[171] The authors suggested a possible different neural organization of reading processes between German and English dyslexic readers. Siok et al.[172] observed the activations patterns of the cortical brain regions of Chinese dyslexic readers on two groups of 16 normal and 16 dyslexic Chinese subjects. Similar to the literature studies on the alphabetic-language dyslexics,[163] reduced gray matter volume as well as reduced functional activation were reported in a left middle frontal gyrus region for the dyslexic group in comparision to the control group. However, no more functional or structural differences were reported in other posterior brain regions that have been shown to be abnormal in the literature for the alphabetic-language dyslexics.[26, 29–32, 35] Seki et al.[169] investigated the functional abnormalities in dyslexic Japanese readers using fMRI. The study analyzed the activation patterns of 5 dyslexic and 5 control children during a reading task of sentences constructed from Japanese phonograms (kana). The left middle temporal gyrus was significantly activated in the control subjects but was less activated in dyslexic subjects. Other activated regions were detected in individual dyslexic subjects. Two dyslexic subjects showed activation in the bilateral occipital cortex. Two other dyslexic subjects showed activation in the inferior part of the frontal regions. The last dyslexic subject exhibited activation in both the bilateral occipital cortex and the inferior part of precentral gyrus. Since other fMRI studies on readers of alphabetic languages showed activation in the superior and middle temporal gyri during semantic tasks,[173, 174] the authors suggested that functional brain abnormality in dyslexia during reading tasks may not differ between languages.[169] Another study by Kita et al.[170] used fMRI to investigate abnormal brain functionality in Japanese dyslexic children. The study analyzed the activation patterns of 14 dyslexic children, 15 control children, and 30 control adults during a phonological manipulation task. The phonological task activated areas in the left inferior and middle frontal gyrus, left superior temporal gyrus, and bilateral basal ganglia. Among these areas, a hyperactivity and hypo-activity were observed in the basal ganglia and the left superior temporal gyrus, respectively, in the dyslexic group as compared to the two other groups. The authors suggested that the abnormal brain activity may have similarities and differences between dyslexic Japanese and other speaking alphabetical languages. Table VI summarizes the current fMRI-based systems for detecting functional abnormalities in dyslexia.

DISCUSSION AND CONCLUSION

Investigating dyslexia-associated brain abnormalities provides insights into the possible pathophysiological mechanisms of the condition. In addition, different neuroimaging modalities offer noninvasive ways for the early detection of dyslexia and for following the outcome of treatment interventions. In this paper, an overview of more than 200 articles that appeared in the field are presented to address the methodologies and findings of the current MRI-based systems for detecting brain abnormalities associated with dyslexia. This paper addresses the strengths and limitations of the current approaches, as well as the current MRI-based methods for dyslexia diagnosis. In the final section, we summarize this work by addressing the correlation between the MRI findings in the literature and outlining the research challenges that face proposed MRI-based diagnostic methods. In addition, the suggested trends to solve these challenges are presented.

Several studies have addressed the correlation between MRI findings in dyslexia by using hybrid MRI techniques (e.g., fMRI supported with structural MRI) or applying meta-analysis on the existing MRI findings in dyslexia. For example, Menghini et al.[36] investigated a possible correlation between fMRI and structural MRI findings associated with the reading process on a group on 10 dyslexic and 10 control subjects. A VBM approach reported reduced grey matter volumes in the right posterior superior parietal lobule and precuneus and in the right supplementary motor area in the brains of dyslexic individuals. The reported structural abnormalities are consistent with the reported fMRI changes in the activation areas of the brain during an implicit learning task. The results support that an impairment of an implicit learning task might affect the ability of learning to read. Hoeft et al.[35] used both fMRI and VBM analysis to compare the structural and functional findings in dyslexia with two judgment control groups: an age-matched group and a younger reading-matched group. They applied fMRI to report the activated areas of the brain during visual word rhyme judgment compared with visual cross-hair fixation rest. Compared to the age-matched group, the dyslexic group reported hypo-activation in left parietal and bilateral fusiform cortices and hyper-activation in left inferior and middle frontal gyri, caudate, and thalamus. Compared to the reading-matched group, the dyslexic group reported hypo activation in left parietal and fusiform regions. The VBM analysis reported reduced gray matter volume in the hypo-activated areas, i.e., only in the left parietal region, suggesting the independence of this area on current reading ability. The results also suggested that the areas of hyper-activation may relate to the level of current reading ability and their independence of atypical brain morphology in dyslexia.

In addition, the correlation between DTI and structural findings has been investigated. Hoeft et al.[175] investigated the capabilities of integrating DTI and fMRI findings to detect future long-term improvement in reading skills. The study, conducted on 25 children with dyslexia, showed that the combination of right inferior frontal gyri activation (observed using fMRI analysis) and right superior longitudinal fasciculus white matter integrity (observed using DTI analysis) predicted with an accuracy of 72% which particular child would improve his/her reading skills 2.5 years later. In addition, the activation patterns across the whole brain during phonological processing increased the prediction accuracy over 90%. These results suggested that MRI findings can predict future behavioral outcomes. Steinbrink et al.[37] reported a decreased FA in bilateral fronto-temporal and left temporo-parietal white matter regions (inferior and superior longitudinal fasciculus) in German dyslexic individuals. A correlation between white matter anisotropy and speed of pseudoword reading was observed.

Moreover, meta-analyses on fMRI findings were applied to assess the consistency of reported findings.[176,177] Maisog et al.[176] performed two activation likelihood estimation (ALE) meta-analyses, one to reveal the over-activations and the other to reveal the under-activations that are associated with dyslexia using either fMRI or PET. The first meta-analysis on six studies[83,178–182] showed hyperactivity in right thalamus and anterior insula of dyslexic individuals. The second meta-analysis on nine studies[83,178–185] showed dyslexia-associated under-activation in two left extrastriatal areas within the Brodmann area 37, precuneus, inferior parietal cortex, superior temporal gyrus, thalamus, and left inferior frontal gyrus and dyslexia-associated hypo-activity in the fusiform, post-central, and superior temporal gyri. The authors suggested that reading tasks are more associated with the left-sided brain regions in control subjects and the right-sided brain regions in dyslexic subjects. The analysis did not support dyslexia-associated abnormalities in the cerebellum or the left frontal cortex, suggesting that these areas may be varied according to the study's design. Richlan et al.[177] performed an ALE meta-analysis of 17 studies (12 fMRI and 5 PET[35,83,180–193]). The lowest under-activations were observed in inferior parietal, superior temporal, middle and inferior temporal, and fusiform regions of the dyslexics' left hemisphere. Over-activation in the primary motor cortex and the anterior insula in dyslexic subjects was associated with under-activation in the inferior frontal gyrus.

Meta-analyses of structural MRI studies (VBM studies) has also been reported, e.g., in Refs. [171, 194]. Richlan et al.[171] performed a coordinate-based meta-analysis on nine VBM studies.[29–37] Reduced gray matter volume was found in the right superior temporal gyrus and left superior temporal sulcus of dyslexic brains, consistently across studies. Correlated reading-related under-activation using fMRI was reported in the left superior temporal sulcus on a previous meta-analyses on functional brain abnormalities in dyslexic readers.[195] These results suggested a correlation between structural and functional MRI for imaging the brain abnormalities in dyslexia. To identify the basis of this correlation and possible overlaps between structural and functional abnormalities in the brains of dyslexic individuals, Linkersdorfer et al.[194] performed two types of meta-analysis: an ALE metaanalysis on nine VBM studies[29–31,33–35,37,43] and an ALE meta-analyses of imaging studies reporting functional under-activations (24 studies[1,35,83,142,168,180–185,187,189–193,196–202]) or over-activations (11 studies[35,83,168,180–182,187,192,193,199,202]) in dyslexia. The VBM meta-analysis reported six significant clusters of altered grey matter volumes in the bilateral temporo-parietal and left occipito-temporal cortical regions and in the cerebellum bilaterally. Areas of overlap between the VBM meta-analysis results and the meta-analyses of functional under and over-activation results were reported in the fusiform and supramarginal gyri of the left hemisphere, and in the left cerebellum, respectively. These results provided evidence for consistent structural brain variations with functional abnormalities in left hemispheric regions. Overall, the studies reporting a correlation between MRI findings may lead to a better understanding of the brain network in dyslexia as well as a better description of how the brain works. In the rest of this section, we will outline the different research challenges that face the MRI-based systems for detecting brain abnormalities associated with dyslexia as well as the suggested trends to solve these challenges.

Research Challenges

Several challenges and aspects face MRI-based systems for detecting the brain abnormalities associated with dyslexia. These challenges can be summarized as follows:

- The findings of structural MRI-based systems face the following challenges:

  —Volumetric approaches depend on the segmentation of anatomical structures (e.g., white matter, grey matter, corpus callosum, planum temporale, and cerebellum). The segmentation of these structures is challenging due to inhomogeneities of the named brain structures. This may affect the accuracy of voxel-based measurements and may thus produce inconsistent findings.

  —A limited number of studies have addressed the role of the planum temporale and cerebellum in developmental dyslexia. More research work should be investigated to provide more accurate findings regarding a possible relation between these structures to developmental dyslexia.

  —More sophisticated shape indexes should be developed to describe morphological variability of brain structures.

  —3D and longitudinal analysis techniques of brain structures are challenging and but necessary to better describe some of the reported brain abnormalities.

- DTI-based systems' findings face the following challenges:

  —More accurate indexes should be investigated to describe the connectivity of the white matter microstructure.

  —DTI-based approaches may help to determine the diffusion parameters of the white matter structure. However, supported structural MRI may be helpful to provide better insights regarding the white matter abnormalities.

  —Longitudinal analysis techniques of DTI images are challenging. However, they may help to better understand the connectivity of the white matter structure in dyslexia.

- The findings of fMRI-based systems face the following challenges:

  —fMRI helps to determine the abnormal activation patterns in dyslexia during different brain operations.

However, supported structural MRI is needed to reveal if this abnormal brain functionality is due to a physical structural abnormality or due to the study's design.
—Longitudinal analysis of fMRI findings are challenging and may help to better understand the abnormal functionality of dyslexic brains.

Therefore, there is a need to develop more efficient systems for obtaining more accurate findings about dyslexia.

Trends

To address the aforementioned challenges, recent trends for the detection of dyslexia associated abnormalities involve the following aspects:

- More powerful, sophisticated shape features of brain structures need further investigations. A recent trend describes the cortex shape by representing its 3D surface with a linear combination of spherical harmonics (SH).[44, 45] Another trend uses a cylindrical map to accurately detect the shape variability between two 3D surfaces[95, 96, 102] (e.g., between CCs of normal and dyslexic subjects). Also, the 3D geometric characteristics of CWM gyrifications between normal and dyslexic subjects has been recently employed.[53–56] A suggested future work is to employ different types of shape features from different brain structures to achieve better detection and diagnosis of dyslexia.
- Integrating the findings of different MRI techniques (e.g., fMRI, DTI, and structural MRI) is very challenging. Studies should investigate the correlation between these findings and the impact of fusing the information obtained from these different types of images. The functional information from fMRI, the shape and anatomical information from structural MRI, and the connectivity information from DTI may lead to a better description of the brain network in dyslexia and illustrate how it works.
- Analysis of MRI findings over long period of time throughout longitudinal studies may give more consistent findings and better insights about dyslexia. In addition, longitudinal studies may help diagnose dyslexia at early stages and provide outcome measures of treatment.

The clinical importance of the detection of dyslexia-associated abnormalities in brain structures has been reflected upon over 200 publications. The challenges and trends presented in this section, suggest that investigating more efficient MRI-based systems for the detection of dyslexia-associated abnormalities in brain structures will remain a very active research area. Thus, more comprehensive studies are necessary for establishing the state-of-the-art MRI-based systems in this active research field.

REFERENCES

1. V. Blau, N. van Atteveldt, M. Ekkebus, R. Goebel, and L. Blomert, Reduced neural integration of letters and speech sounds links phonological and reading deficits in adult dyslexia. *Curr. Biol.* 19, 503 (**2009**).
2. M. J. Snowling, Dyslexia, Blackwell Publishing, Malden (**2000**).
3. K. Pugh, W. Mencl, A. Jenner, L. Katz, S. Frost, J. Lee, S. Shaywitz, and B. Shaywitz, Functional neuroimaging studies of reading and reading disability (developmental dyslexia). *Ment. Retard. Dev. Disabil. Res. Rev.* 6, 61 (**2000**).
4. G. R. Lyon, S. E. Shaywitz, and B. A. Shaywitz, A definition of dyslexia. *Ann. Dyslexia.* 53, 1 (**2003**).
5. J.-F. Démonet, M. J. Taylor, and Y. Chaix, Developmental dyslexia. *Lancet* 363, 1451 (**2004**).
6. F. R. Vellutino, Dyslexia: Theory and Research, MIT Press, Cambridge, MA (**1979**).
7. F. Vellutino and D. Scanlon, Phonological coding, phonological awareness, and reading ability: Evidence from a longitudinal and experimental study. *Merrill. Palmer. Quarterly* 33, 321 (**1987**).
8. U. Frith, Beneath the surface of developmental dyslexia. *Surface Dyslexia* 32, 301 (**1985**).
9. J. Torgesen, Lessons Learned from Research on Interventions for Students Who Experience Difficulty Learning to Read, The Voice of Evidence in Reading Research, edited by P. McCardle and V. Chabra, Paul H Brookes Publishing, Berlin (**1994**), pp. 338–355.
10. D. V. M. Bishop and M. J. Snowling, Developmental dyslexia and specific language impairment: Same or different? *Psychol. Bull.* 130, 858 (**2004**).
11. T. A. Keller and M. A. Just, Altering cortical connectivity: Remediation-induced changes in the white matter of poor readers. *Neuron* 64, 624 (**2009**).
12. S. E. Shaywitz, Dyslexia. *N. Engl. J. Med.* 338, 307 (**1998**).
13. F. Ramus, S. Rosen, S. C. Dakin, B. L. Day, J. M. Castellote, S. White, and U. Frith, Theories of developmental dyslexia: Insights from a multiple case study of dyslexic adults. *Brain* 126, 841 (**2003**).
14. E. Temple, Brain mechanisms in normal and dyslexic readers. *Curr. Opin. Neurobiol.* 12, 178 (**2002**).
15. M. Wolf, Proust and the Squid: The Story and Science of the Reading Brain, Harper Collins, New York (**2007**).
16. M. Casanova and C. R. Tillquist, Encephalization, emergent properties, and psychiatry: A minicolumnar perspective. *Neuroscientist* 14, 101 (**2008**).
17. V. B. Mountcastle, Perpetual Neuroscience: The Cerebral Cortex, Harvard University Press, Cambridge (**1999**).
18. M. Casanova, D. P. Buxhoeveden, M. Cohen, A. E. Switala, and E. L. Roy, Minicolumnar pathology in dyslexia. *Ann. Neurol.* 52, 108 (**2002**).
19. E. L. Williams and M. F. Casanova, Autism and dyslexia: A spectrum of cognitive styles as defined by minicolumnar morphometry. *Med. Hypotheses* 74, 59 (**2010**).
20. M. Casanova, J. Araque, and J. Giedd, Reduced brain size and gyrification in the brains of dyslexic patients. *J. Child Neurol.* 9, 275 (**2004**).
21. G. Eden, The neural basis of developmental dyslexia. *Ann. Dyslexia* 50, 1 (**2000**).
22. Y.-F. Sun, J.-S. Lee, and R. Kirby, Brain imaging findings in dyslexia. *Pediatr. Neonatol.* 51, 89 (**2010**).
23. R. Peterson, L. Robin, and B. F. Pennington, Developmental dyslexia. *Lancet* 379, 1997 (**2012).**
24. P. Mansfield, Imaging by nuclear magnetic resonance. *J. Phys. E. Sci. Instrum.* 21, 18 (**1984**).
25. P. Mansfield, Snapshot magnetic resonance imaging (nobel lecture). *Angew. Chem. Int. Ed.* 43, 5456 (**2004**).
26. M. Eckert, Neuroanatomical markers for dyslexia: A review of dyslexia structural imaging studies. *Neuroscientist* 10, 362 (**2004**).
27. U. Frith, Autism and dyslexia: A glance over 25 years of research. *Perspect. Psychol. Sci.* 8, 670 (**2013**).
28. S. Eliez, J. M. Rumsey, J. N. Giedd, J. E. Schmitt, A. J. Patwardhan, and A. L. Reiss, Morphological alteration of temporal lobe gray matter in dyslexia: An MRI study. *J. Child. Psychol. Psychiatry* 41, 637 (**2000**).

29. M. Kronbichler, H. Wimmer, W. Staffen, F. Hutzler, A. Mair, and G. Ladurner, Developmental dyslexia: Gray matter abnormalities in the occipitotemporal cortex. *Hum. Brain. Mapp.* 29, 613 (**2008**).

30. W. E. Brown, S. Eliez, V. Menon, J. M. Rumsey, C. D. White, and A. L. Reiss, Preliminary evidence of widespread morphological variations of the brain in dyslexia. *Neurology* 56, 781 (**2001**).

31. S. M. Brambati, C. Termine, M. Ruffino, G. Stella, F. Fazio, S. F. Cappa, and D. Perani, Regional reductions of gray matter volume in familial dyslexia. *Neurology* 63, 742 (**2004**).

32. G. Silani, U. Frith, J. F. Demonet, F. Fazio, D. Perani, C. Price, C. D. Frith, and E. Paulesu, Brain abnormalities underlying altered activation in dyslexia: A voxel based morphometry study. *Brain* 128, 2453 (**2005**).

33. M. A. Eckert, C. M. Leonard, M. Wilke, M. Eckert, T. Richards, A. Richards, and V. Berninger, Anatomical signatures of dyslexia in children: Unique information from manual and voxel based morphometry brain measures. *Cortex* 41, 304 (**2005**).

34. E. Vinckenbosch, F. Robichon, and S. Eliez, Gray matter alteration in dyslexia: Converging evidence from volumetric and voxel-by-voxel MRI analyses. *Neuropsychologia* 43, 324 (**2005**).

35. F. Hoeft, A. Meyler, A. Hernandez, C. Juel, H. Taylor-Hill, J. L. Martindale, G. McMillon, G. Kolchugina, J. M. Black, A. Faizi, G. K. Deutsch, W. T. Siok, A. L. Reiss, S. Whitfield-Gabrieli, and J. D. E. Gabrieli, Functional and morphometric brain dissociation between dyslexia and reading ability. *Proc. Natl. Acad. Sci. USA* 104, 4234 (**2007**).

36. D. Menghini, G. E. Hagberg, L. Petrosini, M. Bozzali, E. Macaluso, C. Caltagirone, and S. Vicari, Structural correlates of implicit learning deficits in subjects with developmental dyslexia. *Ann. N. Y. Acad. Sci.* 1145, 212 (**2008**).

37. C. Steinbrink, K. Vogt, A. Kastrup, H.-P. Müller, F. D. Juengling, J. Kassubek, and A. Riecker, The contribution of white and gray matter differences to developmental dyslexia: Insights from DTI and VBM at 3.0 T. *Neuropsychologia* 46, 3170 (**2008**).

38. C. Pernet, J. Andersson, E. Paulesu, and J. F. Demonet, When all hypotheses are right: A multifocal account of dyslexia. *Hum. Brain Mapp.* 30, 2278 (**2009**).

39. R. T. Schultz, N. K. Cho, L. H. Staib, L. E. Kier, J. M. Fletcher, S. E. Shaywitz, D. P. Shankweiler, L. Katz, J. C. Gore, J. S. Duncan, and B. A. Shaywitz, Brain morphology in normal and dyslexic children: The influence of sex and age. *Ann. Neurol.* 35, 732 (**1994**).

40. T. M. Evans, D. L. Flowers, E. M. Napoliello, and G. F. Eden, Sex-specific gray matter volume differences in females with developmental dyslexia. *Brain Struct. Funct.* (**2013**), DOI: 10.1007/s00429-013-0552-4, (in press).

41. K. Jednoróg, N. Gawron, A. Marchewka, S. Heim, and A. Grabowska, Cognitive subtypes of dyslexia are characterized by distinct patterns of grey matter volume. *Brain Struct. Funct.* (**2013**), DOI: 10.1007/s00429-013-0595-6, (in press).

42. A. J. Krafnick, D. L. Flowers, E. M. Napoliello, and G. F. Eden, Gray matter volume changes following reading intervention in dyslexic children. *Neuroimage* 57, 733 (**2011**).

43. N. M. Raschle, M. Chang, and N. Gaab, Structural brain alterations associated with dyslexia predate reading onset. *Neuroimage* 57, 742 (**2011**).

44. M. Nitzken, M. F. Casanova, G. Gimel'farb, A. Elnakib, F. Khalifa, A. Switala, and A. El-Baz, 3D shape analysis of the brain cortex with application to dyslexia, *Proceedings of the International Conference on Image Processing (ICIP'2011)*, Brussels, Belgium, September (**2011**).

45. E. L. Williams, A. El-Baz, M. Nitzken, A. E. Switala, and M. F. Casanova, Spherical harmonic analysis of cortical complexity in autism and dyslexia. *Transl. Neurosci.* 3, 36 (**2012**).

46. I. Altarelli, K. Monzalvo, S. Iannuzzi, J. Fluss, C. Billard, F. Ramus, and G. Dehaene-Lambertz, A functionally guided approach to the morphometry of occipitotemporal regions in developmen- tal dyslexia: Evidence for differential effects in boys and girls. *J. Neurosci.* 33, 11296 (**2013**).

47. M. Nitzken, M. F. Casanova, F. Khalifa, G. Sokhadze, and A. El-Baz, Shape-based detection of cortex variability for more accurate discrimination between autistic and normal brains, Handbook of Multi Modality State-of-the-Art Medical Image Segmentation and Registration Methodologies, edited by A. El-Baz, R. Acharya, A. Laine, and J. Suri, Springer, New York (**2011**), pp. 161–185.

48. M. Nitzken, M. F. Casanova, G. Gimel'farb, F. Khalifa, A. Elnakib, A. E. Switala, and A. El-Baz, 3D shape analysis of the brain cortex with application to autism, *Proceedings of the IEEE International Symposium on Biomedical Imaging: From Nano to Macro (ISBI'2011)*, Chicago, Illinois, USA, March 30–April 2 (**2011**).

49. A. Elnakib, M. Nitzken, M. F. Casanova, H.-Y. Park, G. Gimel'farb, and A. El-Baz, Quantification of Age-Related Brain Cortex Change Using 3D Shape Analysis, *Proceedings of the International Conference on Pattern Recognition (ICPR'2012)*, Tsukuba, Japan, November (**2012**) .

50. A. M. Dale, B. Fischl, and M. I. Sereno, Cortical surface-based analysis: I. segmentation and surface reconstruction. *Neuroimage* 9, 179 (**1999**).

51. B. Fischl and A. M. Dale, Measuring the thickness of the human cerebral cortex from magnetic resonance images. *Proc. Natl. Acad. Sci. USA* 97, 11050 (**2000**).

52. R. D. Fields, White matter in learning, cognition and psychiatric disorders. *Trends. Neurosci.* 31, 361 (**2008**).

53. A. El-Baz, M. Casanova, G. Gimel'farb, M. Mott, A. Switala, E. Vanbogaert, and R. McCracken, Dyslexia diagnostics by 3D texture analysis of cerebral white matter gyrifications, *Proceedings of the International Conference on Pattern Recognition (ICPR'2008)*, Tampa, Florida, USA, December (**2008**).

54. A. El-Baz, M. Casanova, G. Gimel'farb, M. Mott, A. Switala, E. Vanbogaert, and R. McCracken, A new CAD system for early diagnosis of dyslexic brains, *Proceedings of the International Conference on Image Processing (ICIP'2008)*, San Diego, California, USA, October (**2008**).

55. A. El-Baz, M. Casanova, G. Gimelfarb, M. Mott, and A. Switala, An MRI-based diagnostic framework for early diagnosis of dyslexia. *Int. J. CARS.* 3, 181 (**2008**).

56. M. F. Casanova, A. S. El-Baz, J. Giedd, J. M. Rumsey, and A. E. Switala, Increased white matter gyral depth in dyslexia: Implications for corticocortical connectivity. *J. Autism. Dev. Disord.* 40, 21 (**2010**).

57. M. F. Casanova, A. Farag, A. El-Baz, M. Meghan, H. Hassan, R. Fahmi, and A. E. Switala, Abnormalities of the gyral window in autism: A macroscopic correlate to a putative minicolumnopathy. *JSER* 1, 85 (**2007**).

58. R. Fahmi, A. S. El-Baz, H. E. A. E. Munim, A. A. Farag, and M. F. Casanova, Classification techniques for autistic versus typically developing brain using MRI data, *Proceedings of the IEEE International Symposium on Biomedical Imaging: From Nano to Macro (ISBI'2007)*, Washington, DC, USA, April (**2007**).

59. A. El-Baz, M. F. Casanova, G. Gimel'farb, M. Mott, and A. E. Switwala, A new image analysis approach for automatic classification of autistic brains, *Proceedings of the IEEE International Symposium on Biomedical Imaging: From Nano to Macro (ISBI'2007)*, Washington, DC, USA, April (**2007**).

60. A. A. Farag, R. Fahmi, M. F. Casanova, A. E. Abdel-Hakim, H. A. El-Munim, and A. El-Baz, Robust Neuroimaging-Based Classification Techniques of Autistic Versus Typically Developing Brain, Deformable Models, Springer, New York (**2007**), pp. 535–566.

61. R. Fahmi, A. El-Baz, H. Hassan, A. A. Farag, and M. F. Casanova, Structural MRI-based discrimination between autistic and typically developing brain, *Proceedings of the Computer Assisted Radiology and Surgery (CARS'2007)*, Berlin, Germany, June (**2007**).

62. A. El-Baz, M. F. Casanova, G. Gimel'farb, M. Mott, and A. E. Switala, Autism diagnostics by 3D texture analysis of cerebral white matter gyrifications, *Proceedings of the International Conference on Medical Image Computing and Computer-Assisted Intervention (MICCAI'2007)*, Brisbane, Australia **(2007)**, October 29–November 2.

63. M. F. Casanova, A. El-Baz, M. Mott, G. Mannheim, H. Hassan, R. Fahmi, J. Giedd, J. M. Rumsey, A. E. Switala, and A. Farag, Reduced gyral window and corpus callosum size in autism: Possible macroscopic correlates of a minicolumnopathy. *J. Autism. Dev. Disord.* 39, 751 **(2009)**.

64. A. Galaburda, Developmental dyslexia: Current anatomical research. *Ann. Dyslexia.* 33, 41 **(1983)**.

65. A. M. Galaburda, G. F. Sherman, G. D. Rosen, F. Aboitiz, and N. Geschwind, Developmental dyslexia: Four consecutive patients with cortical anomalies. *Ann. Neurol.* 18, 222 **(1985)**.

66. G. W. Hynd, M. Semrud-Clikeman, A. R. Lorys, E. S. Novey, and D. Eliopulos, Brain morphology in developmental dyslexia and attention deficit disorder/hyperactivity. *Arch. Neurol.* 47, 919 **(1990)**.

67. A. A. Beaton, The relation of planum temporale asymmetry and morphology of the corpus callosum to handedness, gender, and dyslexia: A review of the evidence. *Brain Lang.* 60, 255 **(1997)**.

68. K. Hugdahl, E. Heiervang, H. Nordby, A. I. Smievoll, H. Steinmetz, J. Stevenson, and A. Lund, Central auditory processing, MRI morphometry and brain laterality: Applications to dyslexia. *Scand. Audiol.* 27, 26 **(1998)**.

69. M. A. Eckert and C. M. Leonard, Structural imaging in dyslexia: The planum temporale. *Ment. Retard. Dev. Disabil. Res. Rev.* 6, 198 **(2000)**.

70. C. Rae, J. A. Harasty, T. E. Dzendrowskyj, J. B. Talcott, J. M. Simpson, A. M. Blamire, R. M. Dixon, M. A. Lee, C. H. Thompson, P. Styles, A. J. Richardson, and J. F. Stein, Cerebellar morphology in developmental dyslexia. *Neuropsychologia* 40, 1285 **(2002)**.

71. S. K. Laycock, I. D. Wilkinson, L. I. Wallis, G. Darwent, S. H. Wonders, A. J. Fawcett, P. D. Griffiths, and R. I. Nicolson, Cerebellar volume and cerebellar metabolic characteristics in adults with dyslexia. *Ann. N. Y. Acad. Sci.* 1145, 222 **(2008)**.

72. C. J. Stoodley and J. F. Stein, Cerebellar function in developmental dyslexia. *Cerebellum* 12, 267 **(2012)**.

73. J. M. Rumsey, R. Dorwart, M. Vermess, M. B. Denckla, M. J. P. Kruesi, and J. L. Rapoport, Magnetic resonance imaging of brain anatomy in severe developmental dyslexia. *Arch. Neurol.* 43, 1045 **(1986)**.

74. G. W. Hynd and M. Semrud-Clikeman, Dyslexia and brain morphology. *Psychol. Bull.* 106, 447 **(1989)**.

75. R. Duara, A. Kushch, K. Gross-Glenn, W. W. Barker, B. Jallad, S. Pascal, D. A. Loewenstein, J. Sheldon, M. Rabin, B. Levin, and H. Lubs, Neuroanatomic differences between dyslexic and normal readers on magnetic resonance imaging scans. *Arch. Neurol.* 48, 410 **(1991)**.

76. A. Kushch, K. Gross-Glenn, B. Jallad, H. Lubs, M. Rabin, E. Feldman, and R. Duara, Temporal lobe surface area measurements on MRI in normal and dyslexic readers. *Neuropsychologia* 31, 811 **(1993)**.

77. M. A. Dalby, C. C. Elbro, and H. Stødkilde-Jørgensen, Temporal lobe asymmetry and dyslexia: An *in Vivo* study using MRI. *Brain Lang.* 62, 51 **(1998)**.

78. K. E. Watkins, T. Paus, J. P. Lerch, A. Zijdenbos, D. L. Collins, P. Neelin, J. Taylor, K. J. Worsley, and A. C. Evans, Structural asymmetries in the human brain: A voxel-based statistical analysis of 142 MRI scans. *Cereb. Cortex* 11, 868 **(2001)**.

79. J. P. Larsen, T. Høien, I. Lundberg, and H. Ødegaard, MRI evaluation of the size and symmetry of the planum temporale in adolescents with developmental dyslexia. *Brain Lang.* 39, 289 **(1990)**.

80. C. M. Leonard, K. K. S. Voeller, L. J. Lombardino, M. K. Morris, G. W. Hynd, A. W. Alexander, H. G. Andersen, M. Garofalakis, J. C. Honeyman, J. Mao, F. Agee, and E. V. Staab, Anomalous cerebral structure in dyslexia revealed with magnetic resonance imaging. *Arch. Neurol.* 50, 461 **(1993)**.

81. J. S. Bloom, M. A. Garcia-Barrera, C. J. Miller, S. R. Miller, and G. W. Hynd, Planum temporale morphology in children with developmental dyslexia. *Neuropsychologia* 51, 1684 **(2013)**.

82. J. M. Rumsey, B. C. Donohue, D. R. Brady, K. Nace, J. N. Giedd, and P. Andreason, A magnetic resonance imaging study of planum temporale asymmetry in men with developmental dyslexia. *Arch. Neurol.* 54, 1481 **(1997)**.

83. J. M. Rumsey, K. Nace, B. Donohue, D. Wise, J. M. Maisog, and P. Andreason, A positron emission tomographic study of impaired word recognition and phonological processing in dyslexic men. *Arch. Neurol.* 54, 562 **(1997)**.

84. F. Robichon, O. Levrier, P. Farnarier, and M. Habib, Developmental dyslexia: A typical cortical asymmetries and functional significance. *Eur. J. Neurol.* 7, 35 **(2000)**.

85. S. Heim and A. Keil, Large-scale neural correlates of developmental dyslexia. *Eur. Child. Adolesc. Psychiatry* 13, 125 **(2004)**.

86. M. A. Eckert, C. M. Leonard, T. L. Richards, E. H. Aylward, J. Thomson, and V. W. Berninger, Anatomical correlates of dyslexia: Frontal and cerebellar findings. *Brain* 126, 482 **(2003)**.

87. V. G. Fernandez, K. Stuebing, J. Juranek, and J. M. Fletcher, Volumetric analysis of regional variability in the cerebellum of children with dyslexia. *Cerebellum* 12, 906 **(2013)**.

88. J. D. Schmahmann, J. Doyon, M. Petrides, A. C. Evans, and A. W. Toga, MRI Atlas of the Human Cerebellum, Academic Press, San Diego **(2000)**.

89. J. P. Larsen, T. Höien, and H. Ödegaard, Magnetic resonance imaging of the corpus callosum in developmental dyslexia. *Cognitive Neuropsych.* 9, 123 **(1992)**.

90. G. W. Hynd, J. Hall, E. S. Novey, D. Eliopulos, K. Black, J. J. Gonzalez, J. E. Edmonds, C. Riccio, and M. Cohen, Dyslexia and corpus callosum morphology. *Arch. Neurol.* 52, 32 **(1995)**.

91. J. M. Rumsey, M. E. Casanova, G. B. Mannheim, N. Patronas, N. DeVaughn, S. D. Hamburger, and T. Aquino, Corpus callosum morphology, as measured with MRI, in dyslexic men. *Biol. Psychiatry* 39, 769 **(1996)**.

92. F. Robichon and M. Habib, Abnormal callosal morphology in male adult dyslexics: Relationships to handedness and phonological abilities. *Brain Lang.* 62, 127 **(1998)**.

93. J. G. Fine, M. Semrud-Clikeman, T. Z. Keith, L. M. Stapleton, and G. W. Hynd, Reading and the corpus callosum: An MRI family study of volume and area. *Neuropsychology* 21, 235 **(2007)**.

94. K. von Plessen, A. Lundervold, N. Duta, E. Heiervang, F. Klauschen, A. I. Smievoll, L. Ersland, and K. Hugdahl, Less developed corpus callosum in dyslexic subjects—A structural MRI study. *Neuropsychologia* 40, 1035 **(2002)**.

95. M. F. Casanova, A. El-Baz, A. Elnakib, J. Giedd, J. M. Rumsey, E. L. Williams, and A. E. Switala, Corpus callosum shape analysis with application to dyslexia. *Transl. Neurosci.* 1, 124 **(2010)**.

96. A. Elnakib, A. El-Baz, M. F. Casanova, G. Gimel'farb, and A. E. Switala, Image-based detection of corpus callosum variability for more accurate discrimination between dyslexic and normal brains, *Proceedings of the IEEE International Symposium on Biomedical Imaging: From Nano to Macro (ISBI'2010)*, Rotterdam, Netherland, April **(2010)**.

97. A. Elnakib, A. El-Baz, M. F. Casanova, G. Gimel'farb, and A. E. Switala, Image-based detection of corpus callosum variability for more accurate discrimination between autistic and normal brains, *Proceedings of the IEEE International Conference on Image Processing (ICIP'2010)*, Hong Kong, China, September **(2010)**.

98. M. F. Casanova, A. El-Baz, A. Elnakib, A. E. Switala, E. L. Williams, D. L. Williams, N. J. Minshew, and T. E. Conturo, Quantitative analysis of the shape of the corpus callosum in patients with autism and comparison individuals. *Autism* 15, 223 (**2011**).

99. A. El-Baz, A. Elnakib, M. F. Casanova, G. Gimel'farb, A. E. Switala, D. Jordan, and S. Rainey, Accurate automated detection of autism related corpus callosum abnormalities. *J. Med. Sys.* 35, 929 (**2011**).

100. A. Elnakib, M. F. Casanova, G. Gimel'farb, A. E. Switala, and A. El-Baz, Autism diagnostics by centerline-based shape analysis of the corpus callosum, *Proceedings of the IEEE International Symposium on Biomedical Imaging: From Nano to Macro (ISBI'2011)*, Chicago, Illinois, USA (**2011**), March 30–April 2.

101. A. Elnakib, M. F. Casanova, G. Gimel'farb, and A. El-Baz, Autism diagnostics by 3D shape analysis of the corpus callosum, Machine Learning in Computer-aided Diagnosis: Medical Imaging Intelligence and Analysis, edited by K. Suzuki, IGI Global, Hershey (**2012**), pp. 315–335.

102. A. Elnakib, M. F. Casanova, G. Gimelrfarb, A. E. Switala, and A. El-Baz, Dyslexia diagnostics by 3-D shape analysis of the corpus callosum. *IEEE Trans. Inf. Technol. Biomed.* 16, 700 (**2012**).

103. A. Elnakib, A. El-Baz, M. F. Casanova, and A. E. Switala, Dyslexia diagnostics by centerlinebased shape analysis of the corpus callosum, *Proceedings of the International Conference on Pattern Recognition (ICPR'2010)*, Istanbul, Turkey, August (**2010**).

104. D. L. Bihan, J. F. Mangin, C. Poupon, C. A. Clark, S. Pappata, N. Molko, and H. Chabriat, Diffusion tensor imaging: Concepts and applications. *J. Magn. Reson. Imaging* 13, 354 (**2001**).

105. R. Bammer, Basic principles of diffusion-weighted imaging. *Eur. J. Radiol.* 45, 169 (**2003**).

106. P. C. Sundgren, Q. Dong, A. S. K. M. D. Gomez-Hassan, P. Maly, and R. Welsh, Diffusion tensor imaging of the brain: Review of clinical applications. *Neuroradiology* 46, 339 (**2004**).

107. G. K. Deutsch, R. F. Dougherty, R. Bammer, W. T. Siok, J. D. E. Gabrieli, and B. Wandell, Children's reading performance is correlated with white matter structure measured by diffusion tensor imaging. *Cortex* 41, 354 (**2005**).

108. M. Ben-Shachar, R. F. Dougherty, and B. A. Wandell, White matter pathways in reading. *Curr. Opin. Neurobiol.* 17, 258 (**2007**).

109. N. K. Rollins, B. Vachha, P. Srinivasan, J. Chia, J. Pickering, C. W. Hughes, and B. Gimi, Simple developmental dyslexia in children: Alterations in diffusion-tensor metrics of white matter tracts at 3 T1. *Radiology.* 251, 882 (**2009**).

110. R. E. Frye, J. Liederman, K. M. Hasan, A. Lincoln, B. Malmberg, J. McLean, and A. Papanicolaou, Diffusion tensor quantification of the relations between microstructural and macrostructural indices of white matter and reading. *Hum. Brain Mapp.* 32, 1220 (**2011**).

111. T. Schultz, Estimating the crossing of nerve fibers in the human brain, *Proceedings of the SPIE on Electronic Imaging and Signal Processing (SPIE'2009)*, Orlando, Florida, USA, February (**2009**).

112. T. Klingberg, M. Hedehus, E. Temple, T. Salz, J. D. Gabrieli, M. E. Moseley, and R. A. Poldrack, Microstructure of temporo-parietal white matter as a basis for reading ability: Evidence from diffusion tensor magnetic resonance imaging. *Neuron* 25, 493 (**2000**).

113. R. A. Poldrack, A Structural Basis for Developmental Dyslexia: Evidence from Diffusion Tensor Imaging, Dyslexia, Fluency, and the Brain, edited by M. Wolf, York Pr, York, England (**2001**), pp. 213–233.

114. S. N. Niogi and B. D. McCandliss, Left lateralized white matter microstructure accounts for individual differences in reading ability and disability. *Neuropsychologia* 44, 2178 (**2006**).

115. T. Richards, J. Stevenson, J. Crouch, L. C. Johnson, K. Maravilla, P. Stock, R. Abbott, and V. Berninger, Tract-based spatial statistics of diffusion tensor imaging in adults with dyslexia. *Am. J. Neuroradiol.* 29, 1134 (**2008**).

116. J. C. Carter, D. C. Lanham, L. E. Cutting, A. M. Clements-Stephens, X. Chen, M. Hadzipasic, J. Kim, M. B. Denckla, and W. E. Kaufmann, A dual DTI approach to analyzing white matter in children with dyslexia. *Psychiatry Res.* 172, 215 (**2009**).

117. T. N. Odegard, E. A. Farris, J. Ring, R. McColl, and J. Black, Brain connectivity in non-reading impaired children and children diagnosed with developmental dyslexia. *Neuropsychologia* 47, 1972 (**2009**).

118. M. Vandermosten, B. Boets, H. Poelmans, S. Sunaert, J. Wouters, and P. Ghesquière, A tractography study in dyslexia: Neuroanatomic correlates of orthographic, phonological and speech processing. *Brain* 135, 935 (**2012**).

119. M. Vandermosten, B. Boets, H. Poelmans, S. Sunaert, P. Ghesquière, and J. Wouters, White matter lateralization and interhemispheric coherence to auditory modulations in normal reading and dyslexic adults. *Neuropsychologia* 51, 2087 (**2013**).

120. K. M. Hasan, D. L. Molfese, I. S. Walimuni, K. K. Stuebing, A. C. Papanicolaou, P. A. Narayana, and J. M. Fletcher, Diffusion tensor quantification and cognitive correlates of the macrostructure and microstructure of the corpus callosum in typically developing and dyslexic children. *NMR. Biomed.* 25, 1263 (**2012**).

121. T. L. Richards and V. W. Berninger, Brain mapping of language processing using functional MRI connectivity and diffusion tensor imaging, Functional Brain Mapping and the Endeavor to Understand the Working Brain, edited by F. Signorelli and D. Chirchiglia, InTech Publisher, Rijeka, Croatia (**2013**), pp. 77–93.

122. C. Beaulieu, C. Plewes, L. A. Paulson, D. Roy, L. Snook, L. Concha, and L. Phillips, Imaging brain connectivity in children with diverse reading ability. *Neuroimage* 25, 1266 (**2005**).

123. S. L. Rimrodt, D. J. Peterson, M. B. Denckla, W. E. Kaufmann, and L. E. Cutting, White matter microstructural differences linked to left perisylvian language network in children with dyslexia. *Cortex* 46, 739 (**2010**).

124. S. Ogawa, T. M. Lee, A. S. Nayak, and P. Glynn, Oxygenation-sensitive contrast in magnetic resonance image of rodent brain at high magnetic fields. *Magn. Reson. Med.* 14, 68 (**1990**).

125. G. F. Eden and T. A. Zeffiro, Neural systems affected in developmental dyslexia revealed by functional neuroimaging. *Neuron* 21, 279 (**1998**).

126. T. L. Richards, Functional magnetic resonance imaging and spectroscopic imaging of the brain: Application of fMRI and fMRS to reading disabilities and education. *Learn. Disability. Q.* 24, 189 (**2001**).

127. S. E. Shaywitz and B. A. Shaywitz, Dyslexia (specific reading disability). *Biol. Psychiatry* 57, 1301 (**2005**).

128. H. Lyytinen, T. K. Guttorm, T. Huttunen, J. Hämäläinen, P. H. T. Leppänen, and M. Vesterinen, Psychophysiology of developmental dyslexia: A review of findings including studies of children at risk for dyslexia. *J. Neurolinguist.* 18, 167 (**2005**).

129. B. A. Shaywitz, G. R. Lyon, and S. E. S. E. Shaywitz, The role of functional magnetic resonance imaging in understanding reading and dyslexia. *Dev. Neuropsychol.* 30, 613 (**2006**).

130. M. S. Koyama, A. D. Martino, C. Kelly, D. R. Jutagir, J. Sunshine, S. J. Schwartz, F. X. Castellanos, and M. P. Milham, Cortical signatures of dyslexia and remediation: An intrinsic functional connectivity approach. *PLoS One* 8, e55454 (**2013**).

131. S. L. Rimrodt, A. M. Clements-Stephens, K. R. Pugh, S. M. Courtney, P. Gaur, J. J. Pekar, and L. E. Cutting, Functional MRI of sentence comprehension in children with dyslexia: Beyond word recognition. *Cereb. Cortex* 19, 402 (**2009**).

132. H. Baillieux, E. J. M. Vandervliet, M. Manto, P. M. Parizel, P. Deyn, and P. Mariën, Developmental dyslexia and widespread activation across the cerebellar hemispheres. *Brain Lang.* 108, 122 (**2009**).

133. C. Reilhac, C. Peyrin, J.-F. Démonet, and S. Valdois, Role of the superior parietal lobules in letter-identity processing within strings: FMRI evidence from skilled and dyslexic readers. *Neuropsychologia* 51, 601 (**2013**).

134. O. A. Olulade, J. W. Gilger, T. M. Talavage, G. W. Hynd, and C. I. McAteer, Beyond phonological processing deficits in adult dyslexics: A typical fMRI activation patterns for spatial problem solving. *Dev. Neuropsychol.* 37, 617 (**2012**).

135. S. E. Shaywitz, B. A. Shaywitz, K. R. Pugh, R. K. Fulbright, R. T. Constable, W. E. Mencl, D. P. Shankweiler, A. M. Liberman, P. Skudlarski, J. M. Fletcher, L. Katz, C. L. K. E. Marchione, C. Gatenby, and J. C. Gore, Functional disruption in the organization of the brain for reading in dyslexia. *Proc. Natl. Acad. Sci. USA* 95, 2636 (**1998**).

136. B. A. Shaywitz, S. E. Shaywitz, K. R. Pugh, W. E. Mencl, R. K. Fulbright, P. Skudlarski, R. T. Constable, K. E. Marchione, J. M. Fletcher, G. R. Lyon, and J. C. Gore, Disruption of posterior brain systems for reading in children with developmental dyslexia. *Biol. Psychiatry* 52, 101 (**2002**).

137. P. Georgiewa, R. Rzanny, C. Gaser, U.-J. Gerhard, U. Vieweg, D. Freesmeyer, H.-J. Mentzel, A. Kaiser, and B. Blanz, Phonological processing in dyslexic children: A study combining functional imaging and event related potentials. *Neurosci. Lett.* 318, 5 (**2002**).

138. K. Groth, T. Lachmann, A. Riecker, I. Muthmann, and C. Steinbrink, Developmental dyslexics show deficits in the processing of temporal auditory information in German vowel length discrimination. *Read. Writ.* 24, 285 (**2011**).

139. C. Steinbrink, K. Groth, T. Lachmann, and A. Riecker, Neural correlates of temporal auditory processing in developmental dyslexia during German vowel length discrimination: An fMRI study. *Brain Lang.* 121, 1 (**2012**).

140. B. Díaz, F. Hintz, S. J. Kiebel, and K. V. Kriegstein, Dysfunction of the auditory thalamus in developmental dyslexia. *Proc. Natl. Acad. Sci. USA* 109, 13841 (**2012**).

141. I. Kovelman, E. S. Norton, J. A. Christodoulou, N. Gaab, D. A. Lieberman, C. Triantafyllou, M. Wolf, S. Whitfield-Gabrieli, and J. D. E. Gabrieli, Brain basis of phonological awareness for spoken language in children and its disruption in dyslexia. *Cereb. Cortex* 22, 754 (**2012**).

142. V. Blau, J. Reithler, N. van Atteveldt, J. Seitz, P. Gerretsen, R. Goebel, and L. Blomert, Deviant processing of letters and speech sounds as proximate cause of reading failure: A functional magnetic resonance imaging study of dyslexic children. *Brain* 133, 868 (**2010**).

143. G. F. Eden, J. W. VanMeter, J. M. Rumsey, J. M. Maisog, R. P. Woods, and T. A. Zeffiro, Abnormal processing of visual motion in dyslexia revealed by functional brain imaging. *Nature* 382, 66 (**1996**).

144. J. B. Demb, G. M. Boynton, and D. J. Heeger, Functional magnetic resonance imaging of early visual pathways in dyslexia. *J. Neurosci.* 18, 6939 (**1998**).

145. C. Peyrin, M. Lallier, J.-F. Demonet, C. Pernet, M. Baciu, J. F. L. Bas, and S. Valdois, Neural dissociation of phonological and visual attention span disorders in developmental dyslexia: FMRI evidence from two case reports. *Brain Lang.* 120, 381 (**2012**).

146. R. B. H. Tootell, J. B. Reppas, A. M. Dale, R. B. Look, M. I. Sereno, R. Malach, T. J. Brady, and B. R. Rosen, Visual motion aftereffect in human cortical area MT revealed by functional magnetic resonance imaging. *Nature* 375, 139 (**1995**).

147. M.-L. Bosse and S. Valdois, Influence of the visual attention span on child reading performance: A cross-sectional study. *J. Read. Res.* 32, 230 (**2009**).

148. R. C. Wolf, F. Sambataro, C. Lohr, C. Steinbrink, C. Martin, and N. Vasic, Functional brain network abnormalities during verbal working memory performance in adolescents and young adults with dyslexia. *Neuropsychologia* 48, 309 (**2010**).

149. H. Beneventi, F. E. Tønnessen, and L. Ersland, Dyslexic children show short-term memory deficits in phonological storage and serial rehearsal: An fMRI study. *Int. J. Neurosci.* 119, 2017 (**2009**).

150. H. Beneventi, F. E. Tønnessen, L. Ersland, and K. Hugdahl, Executive working memory processes in dyslexia: Behavioral and fMRI evidence. *Scand. J. Psychol.* 51, 192 (**2010**).

151. K. R. Pugh, W. E. Mencl, B. A. Shaywitz, S. E. Shaywitz, R. K. Fulbright, R. T. Constable, P. Skudlarski, K. E. Marchione, A. R. Jenner, J. M. Fletcher, A. M. Liberman, D. P. Shankweiler, L. Katz, C. Lacadie, and J. C. Gore, The angular gyrus in developmental dyslexia: Task-specific differences in functional connectivity within posterior cortex. *Psychol. Sci.* 11, 51 (**2000**).

152. V. Quaglino, B. Bourdin, G. Czternasty, P. Vrignaud, S. Fall, M. E. Meyer, P. Berquin, B. Devauchelle, and G. de Marco, Differences in effective connectivity between dyslexic children and normal readers during a pseudoword reading task: An fMRI study. *Neurophysiol. Clin.* 38, 73 (**2008**).

153. S. van der Mark, P. Klaver, K. Bucher, U. Maurer, E. Schulz, S. Brem, E. Martin, and D. Brandeis, The left occipitotemporal system in reading: Disruption of focal fMRI connectivity to left inferior frontal and inferior parietal language areas in children with dyslexia. *Neuroimage* 54, 2426 (**2011**).

154. L. Cohen, S. Dehaene, L. Naccache, S. Lehéricy, G. Dehaene-Lambertz, M.-A. Hénaff, and F. Michel, The visual word form area spatial and temporal characterization of an initial stage of reading in normal subjects and posterior split-brain patients. *Brain* 123, 291 (**2000**).

155. E. Temple, R. A. Poldrack, A. Protopapas, S. Nagarajan, T. Salz, P. Tallal, M. M. Merzenich, and J. D. E. Gabrieli, Disruption of the neural response to rapid acoustic stimuli in dyslexia: Evidence from functional MRI. *Proc. Natl. Acad. Sci. USA* 97, 13907 (**2000**).

156. W. Backes, E. Vuurman, R. Wennekes, P. Spronk, M. Wuisman, J. van Engelshoven, and J. Jolles, A typical brain activation of reading processes in children with developmental dyslexia. *J. Child. Neurol.* 17, 867 (**2002**).

157. A. Karni, I. A. Morocz, T. Bitan, S. Shaul, T. Kushnir, and Z. Breznitz, An fMRI study of the differential effects of word presentation rates (reading acceleration) on dyslexic readers' brain activity patterns. *J. Neurolinguist* 18, 197 (**2005**).

158. N. Gaab, J. D. E. Gabrieli, G. K. Deutsch, P. Tallal, and E. Temple, Neural correlates of rapid auditory processing are disrupted in children with developmental dyslexia and ameliorated with training: An fMRI study. *Restor. Neurol. Neurosci.* 25, 295 (**2007**).

159. S. Heim, M. Grande, J. Pape-Neumann, M. van Ermingen, E. Meffert, A. Grabowska, W. Huber, and K. Amunts, Interaction of phonological awareness and magnocellular processing during normal and dyslexic reading: Behavioural and fMRI investigations. *Dyslexia* 16, 258 (**2010**).

160. S. Ruff, N. Marie, P. Celsis, D. Cardebat, and J.-F. Démonet, Neural substrates of impaired categorical perception of phonemes in adult dyslexics: An fMRI study. *Brain Cogn.* 53, 331 (**2003**).

161. S. L. Small, D. K. Flores, and D. C. Noll, Different neural circuits subserve reading before and after therapy for acquired dyslexia. *Brain Lang.* 62, 298 (**1998**).

162. E. Temple, G. K. Deutsch, R. A. Poldrack, S. L. Miller, P. Tallal, M. M. Merzenich, and J. D. E. Gabrieli, Neural deficits in children with dyslexia ameliorated by behavioral remediation: Evidence from functional MRI. *Proc. Natl. Acad. Sci. USA* 100, 2860 (**2003**).

163. E. H. Aylward, T. L. Richards, V. W. Berninger, W. E. Nagy, K. M. Field, A. C. Grimme, A. L. Richards, J. B. Thomson, and S. C. Cramer, Instructional treatment associated with changes in brain activation in children with dyslexia. *Neurology* 61, 212 (**2003**).

164. T. L. Richards, E. H. Aylward, V. W. Berninger, K. M. Field, A. C. Grimme, A. L. Richards, and W. Nagy, Individual fMRI activation in orthographic mapping and morpheme mapping after orthographic or morphological spelling treatment in child dyslexics. *J. Neurolinguist* 19, 56 (**2006**).

165. T. L. Richards and V. W. Berninger, Abnormal fMRI connectivity in children with dyslexia during a phoneme task: Before but not after treatment. *J. Neurolinguist* 21, 294 (**2008**).

166. G. F. Eden, K. M. Jones, K. Cappell, L. Gareau, F. B. Wood, T. A. Zeffiro, N. A. E. Dietz, J. A. Agnew, and D. L. Flowers, Neural changes following remediation in adult developmental dyslexia. *Neuron* 44, 411 (**2004**).

167. Y. Zhang, S. Whitfield-Gabrieli, J. A. Christodoulou, and J. D. E. Gabrieli, A typical balance between occipital and fronto-parietal activation for visual shape extraction in dyslexia. *PLoS One* 8, e67331 (**2013**).

168. H. Wimmer, M. Schurz, D. Sturm, F. Richlan, J. Klackl, M. Kronbichler, and G. Ladurner, A dual-route perspective on poor reading in a regular orthography: An fMRI study. *Cortex* 46, 1284 (**2010**).

169. A. Seki, T. Koeda, S. Sugihara, M. Kamba, Y. Hirata, T. Ogawa, and K. Takeshita, A functional magnetic resonance imaging study during sentence reading in Japanese dyslexic children. *Brain Dev.* 23, 312 (**2001**).

170. Y. Kita, H. Yamamoto, K. Oba, Y. Terasawa, Y. Moriguchi, H. Uchiyama, A. Seki, T. Koeda, and M. Inagaki, Altered brain activity for phonological manipulation in dyslexic Japanese children. *Brain* 136, 3696 (**2013**).

171. F. Richlan, M. Kronbichler, and H. Wimmer, Structural abnormalities in the dyslexic brain: A meta-analysis of voxel-based morphometry studies. *Hum. Brain Mapp* (**2012**).

172. W. T. Siok, Z. Niu, Z. Jin, C. A. Perfetti, and L. H. Tan, A structural-functional basis for dyslexia in the cortex of Chinese readers. *Proc. Natl. Acad. Sci. USA* 105, 5561 (**2008**).

173. J. R. Binder, Neuroanatomy of language processing studied with functional MRI. *Clin. Neurosci.* 4, 87 (**1997**).

174. K. R. Pugh, B. A. Shaywitz, S. E. Shaywitz, R. T. Constable, P. Skudlarski, R. K. Fulbright, A. Bronen, D. P. Shankweiler, L. Katz, J. M. Fletcher, and J. C. Gore, Cerebral organization of component processes in reading. *Brain* 119, 1221 (**1996**).

175. F. Hoeft, B. D. McCandliss, J. M. Black, A. Gantman, N. Zakerani, C. Hulme, H. Lyytinen, Whitfield-Gabrieli, G. H. Glover, A. L. Reiss, and J. D. E. Gabrieli, Neural systems predicting long-term outcome in dyslexia. *Proc. Natl. Acad. Sci. USA* 108, 361 (**2011**).

176. J. M. Maisog, E. R. Einbinder, D. L. Flowers, P. E. Turkeltaub, and G. F. Eden, A meta-analysis of functional neuroimaging studies of dyslexia. *Ann. N. Y. Acad. Sci.* 1145, 237 (**2008**).

177. F. Richlan, M. Kronbichler, and H. Wimmer, Functional abnormalities in the dyslexic brain: A quantitative meta-analysis of neuroimaging studies. *Hum. Brain Mapp.* 30, 3299 (**2009**).

178. J. M. Rumsey, B. Horwitz, B. C. Donohue, K. Nace, J. M. Maisog, and P. Andreason, Phonological and orthographic components of word recognition. A PET-rCBF study. *Brain* 120, 739 (**1997**).

179. N. Brunswick, E. McCrory, C. J. Price, C. D. Frith, and U. Frith, Explicit and implicit processing of words and pseudowords by adult developmental dyslexics a search for wernicke's wortschatz? *Brain* 122, 1901 (**1999**).

180. P. Georgiewa, R. Rzanny, J.-M. Hopf, R. Knab, V. Glauche, W.-A. Kaiser, and B. Blanz, fMRI during word processing in dyslexic and normal reading children. *Neuroreport.* 10, 3459 (**1999**).

181. M. Ingvar, P. Af Trampe, T. Greitz, L. Eriksson, S. Stone-Elander, and C. von Euler, Residual differences in language processing in compensated dyslexics revealed in simple word reading tasks. *Brain Lang.* 83, 249 (**2002**).

182. C. Grüling, M. Ligges, R. Huonker, M. Klingert, H.-J. Mentzel, R. Rzanny, W. A. Kaiser, H. Witte, and B. Blanz, Dyslexia: The possible benefit of multimodal integration of fMRI-and EEG-data. *J. Neural Transm.* 111, 951 (**2004**).

183. E. Paulesu, U. Frith, M. Snowling, A. Gallagher, J. Morton, R. S. J. Frackowiak, and C. D. Frith, Is developmental dyslexia a disconnection syndrome? Evidence from PET scanning. *Brain* 119, 143 (**1996**).

184. E. Paulesu, J.-F. Démonet, F. Fazio, E. McCrory, V. Chanoine, N. Brunswick, S. F. Cappa, G. Cossu, M. Habib, C. D. Frith, and U. Frith, Dyslexia: Cultural diversity and biological unity. *Science* 291, 2165 (**2001**).

185. E. J. McCrory, A. Mechelli, U. Frith, and C. J. Price, More than words: A common neural basis for reading and naming deficits in developmental dyslexia? *Brain* 128, 261 (**2005**).

186. E. Schulz, U. Maurer, S. van der Mark, K. Bucher, S. Brem, E. Martin, and D. Brandeis, Impaired semantic processing during sentence reading in children with dyslexia: Combined fMRI and ERP evidence. *Neuroimage* 41, 153 (**2008**).

187. J. R. Booth, G. Bebko, D. D. Burman, and T. Bitan, Children with reading disorder show modality independent brain abnormalities during semantic tasks. *Neuropsychologia* 45, 775 (**2007**).

188. A. Meyler, T. A. Keller, V. L. Cherkassky, D. Lee, F. Hoeft, S. Whitfield-Gabrieli, J. D. E. Gabrieli, and M. A. Just, Brain activation during sentence comprehension among good and poor readers. *Cereb. Cortex* 17, 2780 (**2007**).

189. F. Hoeft, A. Hernandez, G. McMillon, H. Taylor-Hill, J. L. Martindale, A. Meyler, T. A. Keller, W. T. Siok, G. K. Deutsch, M. A. Just, S. Whitfield-Gabrieli1, and J. D. E. Gabrieli1, Neural basis of dyslexia: A comparison between dyslexic and nondyslexic children equated for reading ability. *J. Neurosci.* 26, 10700 (**2006**).

190. S. M. Brambati, C. Termine, M. Ruffino, M. Danna, G. Lanzi, G. Stella, S. F. Cappa, and D. Perani, Neuropsychological deficits and neural dysfunction in familial dyslexia. *Brain Res.* 1113, 174 (**2006**).

191. F. Cao, T. Bitan, T.-L. Chou, D. D. Burman, and J. R. Booth, Deficient orthographic and phonological representations in children with dyslexia revealed by brain activation patterns. *J. Child. Psychol. Psychiatry* 47, 1041 (**2006**).

192. M. Kronbichler, F. Hutzler, W. Staffen, A. Mair, G. Ladurner, and H. Wimmer, Evidence for a dysfunction of left posterior reading areas in German dyslexic readers. *Neuropsychologia* 44, 1822 (**2006**).

193. E. Temple, R. A. Poldrack, J. Salidis, G. K. Deutsch, P. Tallal, M. M. Merzenich, and J. D. E. Gabrieli, Disrupted neural responses to phonological and orthographic processing in dyslexic children: An fMRI study. *Neuroreport* 12, 299 (**2001**).

194. J. Linkersdöfer, J. Lonnemann, S. Lindberg, M. Hasselhorn, and C. J. Fiebach, Grey matter alterations co-localize with functional abnormalities in developmental dyslexia: An ALE metaanalysis. *PLoS One* 7, e43122 (**2012**).

195. F. Richlan, M. Kronbichler, and H. Wimmer, Meta-analyzing brain dysfunctions in dyslexic children and adults. *Neuroimage* 56, 1735 (**2011**).

196. U. Maurer, E. Schulz, S. Brem, S. van der Mark, K. Bucher, E. Martin, and D. Brandeis, The development of print tuning in children with dyslexia: Evidence from longitudinal ERP data supported by fMRI. *Neuroimage* 57, 714 (**2011**).

197. C. Pecini, L. Biagi, D. Brizzolara, P. Cipriani, M. C. D. Lieto, A. Guzzetta, M. Tosetti, and A. M. Chilosi, How many functional brains in developmental dyslexia? When the history of language delay makes the difference. *Cogn. Behav. Neurol.* 24, 85 (**2011**).

198. W. Hu, H. L. Lee, Q. Zhang, T. Liu, L. B. Geng, M. L. Seghier, C. Shakeshaft, T. Twomey, D. W. Green, Y. M. Yang, and C. J. Price, Developmental dyslexia in Chinese and English populations: Dissociating the effect of dyslexia from language differences. *Brain* 133, 1694 (**2010**).

199. F. Richlan, D. Sturm, M. Schurz, M. Kronbichler, G. Ladurner, and H. Wimmer, A common left occipito-temporal dysfunction in developmental dyslexia and acquired letter-by-letter reading? *PLoS One* 5, e12073 (**2010**).

200. E. Schulz, U. Maurer, S. van der Mark, K. Bucher, S. Brem, E. Martin, and D. Brandeis, Reading for meaning in dyslexic and young children: Distinct neural pathways but common endpoints. *Neuropsychologia* 47, 2544 **(2009)**.

201. S. V. der Mark, K. Bucher, U. Maurer, E. Schulz, S. Brem, J. Buckelmüller, M. Kronbichler, T. Loenneker, P. Klaver, E. Martin, and D. Brandeis, Children with dyslexia lack multiple specializations along the visual word-form (VWF) system. *Neuroimage* 47, 1940 **(2009)**.

202. A. Meyler, T. A. Keller, V. L. Cherkassky, J. D. E. Gabrieli, and M. A. Just, Modifying the brain activation of poor readers during sentence comprehension with extended remedial instruction: A longitudinal study of neuroplasticity. *Neuropsychologia* 46, 2580 **(2008)**.